UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2021
or

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to
Commission file number: 001-36866

Summit Therapeutics Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**37-1979717**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
One Broadway, 14th Floor **Cambridge, MA**	**02142**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 514-7149
(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.01 per share	**SMMT**	**The Nasdaq Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No ☒

The aggregate market value of the voting common stock held by non-affiliates based on the closing stock price on June 30, 2021, was $186.0 million. For purposes of this computation only, all executive officers and directors have been deemed affiliates.

The number of outstanding shares of the registrant's common stock, par value $0.01 per share, as of March 10, 2022 was 98,122,356.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement to be filed with the Securities and Exchange Commission within 120 days after registrant's fiscal year ended December 31, 2021 are incorporated by reference into Part III of this report.

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INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 regarding the future financial performance, business prospects and growth of Summit Therapeutics Inc., that involve substantial risks and uncertainties. All statements contained in this Annual Report on Form 10-K, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the timing and evaluation of next steps with respect to our lead product candidate, ridinilazole (formerly SMT19969), for the treatment of patients with *Clostridioides difficile* infection (formerly known as *Clostridium difficile* infection) based upon our review of the topline results for the Phase III Ri-CoDIFy study announced in December 2021, including exploring potential partnership opportunities;
- the timing of and the ability to obtain marketing approval of ridinilazole, and the ability of ridinilazole to meet existing or future regulatory standards;
- the timing and conduct of clinical trials for any other product candidates;
- the potential benefits of our Discuva Platform to identify new bacterial targets for drug discovery and development;
- our plans to conduct research and development and advance potential new mechanism antibiotic compounds identified and developed under our Discuva Platform;
- the potential benefits and future operation of our collaboration with the Biomedical Advanced Research and Development Authority, or BARDA;
- the potential benefits and future operation of our license and commercialization agreement with Eurofarma Laboratórios SA, or Eurofarma;
- our plans with respect to possible future collaborations and partnering arrangements;
- our plans to pursue research and development of other future product candidates;
- the potential advantages of ridinilazole and our other new mechanism antibiotics;
- the rate and degree of market acceptance and clinical utility of ridinilazole and our other new mechanism antibiotics;
- our estimates regarding the potential market opportunity for ridinilazole and our other new mechanism antibiotics;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of ridinilazole;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- our competitive position;
- the need to raise additional capital to fund ongoing operations and capital needs; and
- the impact of the novel coronavirus pandemic (COVID-19) and the response to it.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Report, particularly in the “Risk Factors” in Part 1, Item 1A of this Annual Report on Form 10-K, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

SUMMARY OF RISK FACTORS

Summary

Below is a summary of the principal factors that make an investment in Summit Therapeutics Inc. speculative or risky. The following summary does not contain all of the information that may be important to you, and you should read the below summary in conjunction with the more detailed discussion of risks set forth under the heading "Risk Factors" in Part I, Item IA of this Annual Report on Form 10-K.

Risks Related to Our Financial Position and Need for Additional Capital

- We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never generate profits from operations or maintain profitability.
- We will require substantial additional capital to fund our operations and if we fail to obtain necessary financing we will not be able to complete the development and commercialization of our product candidates.

Risks Related to our Financial Dependence on Third Parties

- Our reliance on government funding for ridinilazole adds uncertainly to our research and commercialization efforts, and may impose requirements that increase the costs of commercialization and production of product candidates developed with the support of government-funded programs in which we participate.

Risks Related to Continuing Development of and Next Steps for Our Product Candidates

- We depend heavily on the success of our lead product candidate, ridinilazole, which we are developing for the treatment of CDI, and our second product candidate, SMT-738. Based on our evaluation of the results of the Ri-CoDIFy clinical trial for ridinilazole and our determinations with respect to how to proceed, including potentially seeking third-party partnership opportunities on terms that meet our requirements, we may extend the period in which we will incur significant financial losses as an organization.
- If we are able to enter into one or more such third party partnership arrangements, we may be subject to the third parties' handling of activities, such as the commercialization of ridinilazole, and we may have limited control over the final development, marketing and commercialization of our product candidates.

Risks Related to Our Industry and Market

- We face substantial competition, which may result in others discovering, developing or commercializing products before us or more successfully than we do.

Risks Related to the Development and Commercialization of our Product Candidates

- We can provide no assurance that our clinical product candidates, including our lead product candidate, ridinilazole, will obtain regulatory approval or that the results of clinical studies will be favorable.
- Drug discovery and development is a complex, time-consuming and expensive process that is fraught with risk and a high rate of failure.
- We depend on our senior management and key personnel for our success, and if we fail to retain such personnel we may experience substantial harm to our business.
- We may depend on collaborations with third parties for the development and commercialization of some of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

Legal, Tax, Regulatory and Compliance Risks

- Our ability to commercialize any of our product candidates is subject to substantial regulatory and legislative uncertainty, including as to pricing, reimbursement practices or other healthcare initiatives which could harm our business.
- We may face costly legal claims, in particular related to product liability and intellectual property infringement.
- We are subject to certain U.S., U.K. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

Risks Related to Our Intellectual Property

- We rely upon patents to protect our technology. We may be unable to protect our intellectual property rights and we may be liable for infringing the intellectual property rights of others.

Risks Related to Corporate Governance

- Our Chief Executive Officer owns more than a majority of the voting power of the outstanding shares of our common stock, and as a result investors may have limited ability to affect either the corporate governance of the Company or the taking of certain major decisions.

Risks Related to Owning Our Common Stock

- Substantial future sales of our shares of common stock in the public market, or the perception that these sales could occur, could cause the price of the shares to decline significantly, even if our business is doing well.
- The prices of our shares of common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

SPECIAL NOTE REGARDING THE REDOMICILIATION

On September 18, 2020, Summit Therapeutics Inc., a Delaware corporation, or New Summit, became the successor issuer to Summit Therapeutics plc, a public limited company incorporated under the laws of England and Wales with the Registrar of Companies of England and Wales, United Kingdom, or Old Summit, for certain purposes under both the Securities Act of 1933, as amended, and the Securities Exchange Act of 1934, as amended, or the Exchange Act. Such succession occurred pursuant to a scheme of arrangement under UK law, which resulted in New Summit becoming the holding company of Old Summit (the predecessor registrant and former holding company) and its subsidiaries, which we refer to as the Redomiciliation Transaction (or "Redomiciliation"). On September 18, 2020, Old Summit was converted into a private limited company under the laws of England and Wales and renamed Summit Therapeutics Limited.

Unless the context requires otherwise, all references in this Report to "Summit," "the Summit Group," "the Company," "we," "ours," "us," or similar terms on or prior to September 18, 2020 (the effective date of the Redomiciliation Transaction), refer to our predecessor, Summit Therapeutics plc, together with its subsidiaries.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the discovery, development, and commercialization of patient-, physician-, caregiver- and societal-friendly medicinal therapies intended to improve quality of life, increase life expectancy, and resolve serious unmet needs. Our novel mechanism pipeline of product candidates is designed with the goal to become the patient-friendly, new-era standard-of-care medicines, and to work in harmony with the human microbiome. Summit's lead product candidate, ridinilazole, is a novel first-in-class drug that is engaged in a global Phase III clinical trial program. On December 20, 2021, we announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole for treating patients suffering from *Clostridioides difficile* infection, also known as *C. difficile* infection, or CDI. Our second product candidate, SMT-738, was announced in May 2021 for combating multidrug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. SMT-738 is the first of a novel class of precision antibiotics that has entered into preclinical development. We intend to expand our portfolio by developing further new mechanism, new era product offerings that are designed to work in harmony with the human gut microbiome in the therapeutic areas of oncology and infectious diseases.

Throughout the process of our clinical development of ridinilazole, we have learned a substantial amount regarding the importance of the microbiome as we have sought to reduce *C. difficile* infection recurrence to the lowest practical levels. Importantly, as we have continued to intensify our focus on the microbiome, we believe that the focus on the health of the microbiome will become one of the most important developments in human health over the next decade. As a result, we intend to implement a strategy that primarily centers on microbiome-focused therapeutics that could benefit treatments in the areas of oncology and anti-infectives. We will enact this focus through business development activities, including possible acquisitions of and/or collaborations with existing entities.

For ridinilazole, we are in the process of evaluating the future path forward, including potential partnership opportunities.

Ridinilazole for Clostridioides difficile Infection

Our lead CDI product candidate is ridinilazole (formerly SMT19969), an orally administered, novel mechanism, small molecule antibiotic. The first patient in our Phase III clinical program was dosed ridinilazole in February 2019. The Phase III clinical program consists of two Phase III pivotal clinical trials ("Ri-CoDIFy 1" and "Ri-CoDIFy 2") which were combined into a single study ("Ri-CoDIFy"). The Phase III clinical program also consists of a pediatrics study ("Ri-CoDIFy 3"). The Phase III Ri-CoDIFy pivotal trial was designed to assess, as the primary endpoint, the superiority of ridinilazole compared to vancomycin in Sustained Clinical Response ("SCR"), which was defined as Clinical Response of the treated episode of CDI and no recurrence of CDI through 30 days after the end of treatment. Additional endpoints included Clinical Response ("CR"), recurrence rate, safety and tolerability, analyses of the gut microbiome and metabolome, in addition to quality of life and health economic outcome measures. The top-line results of the Ri-CoDIFy study showed that ridinilazole resulted in a numerically higher SCR rate than vancomycin but did not meet the study's primary endpoint threshold for superiority. Patients treated with ridinilazole, a precision antibiotic, experienced substantially less recurrence of *C. difficile* infection as compared to patients administered vancomycin (nominal p-value = 0.0002). It further showed that ridinilazole was well tolerated, and the overall safety profile remained unchanged.

We are in the process of evaluating the future path forward with respect to ridinilazole, including potential partnership opportunities.

Ridinilazole is designed to selectively target the bacterium *Clostridioides difficile* (previously known as *Clostridium difficile*) or *C. difficile* while preserving the commensal microbes of the gut microbiome, thus allowing more rapid restoration of the microbiome to a healthy state. A healthy, diverse microbiome is associated with decreased CDI recurrence rates.

CDI is a bacterial infection of the colon caused by the bacterium *C. difficile* which produces toxins that cause inflammation of the colon resulting in severe watery diarrhea, painful abdominal cramping, nausea, fever, and dehydration. CDI can also result in more serious disease complications, including bowel perforation, sepsis, and death. CDI typically develops following the use of antibiotics that can cause widespread damage to the microbiome, or the natural gut flora, and allow overgrowth of *C. difficile* bacteria. CDI represents a serious healthcare issue in hospitals, long-term care homes, and in the wider community. CDI is the most common healthcare-associated infection.

Ridinilazole's Phase III clinical program has been funded in part with federal funds from the Biomedical Advanced Research and Development Authority ("BARDA"), part of the Office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services. The awarded contract was originally worth up to $62.0 million. In June 2019 and again in January 2020, BARDA increased the value of the contract such that it is now worth up to $72.5 million. The

remaining federal government funding is dependent on BARDA at its sole discretion exercising the final independent option work segment, under our achievement of certain agreed-upon milestones for ridinilazole. As of December 31, 2021, an aggregate of $56.5 million of the total committed BARDA funding has been received.

We have also entered into a license and commercialization agreement with Eurofarma Laboratórios S.A., or Eurofarma, pursuant to which we granted Eurofarma exclusive rights to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean. We have retained commercial rights to ridinilazole for the treatment of CDI across Rest of World territories.

Other Pipeline Product Candidates

Discuva Platform

In December 2017, we expanded our activities in the field of infectious diseases with the acquisition of Discuva Limited, a privately held United Kingdom-based company. Through this acquisition, we obtained a bacterial genetics platform and a suite of software-based technologies (collectively termed our "Discuva Platform"), which facilitate the discovery and development of new mechanism antibiotics. Our Discuva Platform can be used to identify new bacterial targets for drug discovery, understand the mechanism of action of small molecules targeting varying types of bacteria and select the most optimal preclinical candidates, including those with the least propensity to develop bacterial resistance.

In addition to discovery project support, our deep biology and microbiology expertise has been utilized over the past year to provide further insights into the mechanism of action of ridinilazole and to characterize the preclinical microbiology of ridinilazole in greater detail. The mechanism of action and microbiology studies may be an important component of any regulatory filings and communications with regulatory agencies for ridinilazole.

Enterobacteriaceae Program

We continue to advance our highly innovative program targeting infections caused by Enterobacteriaceae. We have used our Discuva Platform to identify our DDS-04 series, a novel chemotype active against a clinically unexploited bacterial target that has the potential to treat Enterobacteriaceae infections. Enterobacteriaceae are a family of bacteria responsible for serious infections across a number of conditions including bloodstream infections, urinary tract infections ("UTI") and hospital-acquired pneumonias. Multi-drug resistant ("MDR") Enterobacteriaceae are resistant to treatment by most or occasionally all existing antibiotics. The most difficult to treat among them are the Extended Spectrum Beta-Lactamase ("ESBL")-producing and the Carbapenem-resistant Enterobacteriaceae ("CRE"). According to the Center for Disease Control and Prevention ("CDC"), ESBL-producing and CRE Enterobacteriaceae have collectively caused an estimated 197,400 infections and 9,100 deaths in hospitalized patients in the United States in 2019. Our DDS-04 series continues to build on highly promising preclinical *in vivo* efficacy data with an immediate focus on a new antibiotic agent for the treatment of complicated urinary tract infections, pneumonia and the associated bacteremia.

Our lead preclinical candidate for the Enterobacteriaceae program from the DDS-04 series is SMT026738 (formerly "DIS-0104145" and referred to as "SMT-738"). SMT-738 is a novel small molecule inhibitor of the essential bacterial lipoprotein transport system (LolCDE) in Gram-negative bacteria, which displays a narrow spectrum of activity towards Enterobacteriaceae. SMT-738 has demonstrated potent *in vitro* activity against global MDR isolates of *E. coli* and *K. pneumoniae,* including the clinically challenging NDM-carrying CRE isolates where many currently available treatment options have succumbed to clinical resistance including colistin, an antibiotic of last resort. Most importantly, SMT-738 has also shown robust *in vivo* efficacy in relevant murine models of UTI, pneumonia and sepsis. A preliminary rodent toxicity study has been concluded and the data supports the continued clinical development of SMT-738. SMT-738 has the potential to become a first in class antibiotic to treat life-threatening infections.

Summit has received a sub-award from CARB-X to progress SMT-738 through preclinical development and an option to continue into Phase Ia clinical studies. The award commits initial non-dilutive funding of up to $4.1 million for the preclinical phase, with the potential for a further $3.7 million available for the continued clinical development upon successfully achieving key preclinical development milestones.

We have been and plan to continue to perform IND-enabling activities.

Our Product Development Pipeline

The following table summarizes our product development pipeline.

Program	Discovery	IND Enabling	Phase I	Phase II	Phase III	Remarks
Clostridioides difficile Infection (CDI)						
Ridinilazole (1) (formerly SMT19969)			*Qualified Infectious Disease Product Designation (FDA)* *Fast Track Designation (FDA)*			Assessing Phase III topline results announced in December 2021.
Carbapenem-resistant Enterobacteriaceae Infection (CRE)						
SMT-738 (2)						Candidate announced in May 2021; IND enabling studies and CMC API manufacture in progress towards GLP toxicity studies

(1) We have granted Eurofarma (see further discussion below of funding arrangement) an exclusive license to the commercial rights for ridinilazole in specified countries in South America, Central America and the Caribbean. We retain commercialization rights across Rest of World territories.
(2) Currently supported by funding from CARB-X (see further discussion below of funding arrangement).

Our Strategy

Our goal is to become a fully integrated biopharmaceutical company focused on the discovery, development, and, commercialization of patient-, provider-, novel mechanism of action and/or new era products that work in harmony with the human gut microbiome, including innovative therapeutics for the treatment of certain cancers and infectious diseases. We have announced our intention to continue to expand our pipeline with therapeutics that work in conjunction with the human gut microbiome for the treatment of certain cancers and infectious diseases through business development activities including, but not limited to, partnerships with, collaborations with, and/or acquisitions of existing entities.

The key elements of our strategy to achieve this goal are to:

Evaluating the future path forward for our existing pipeline product candidates, including potential partnership opportunities, as applicable.

For ridinilazole, we are in the process of evaluating the future path forward, including potential partnership opportunities.

Expand our product portfolio of patient-friendly, new-era standards-of-care through our Summit Therapeutics Innovation Engine, including expanding our pipeline to potentially include patient-friendly oncology treatments.

We intend to expand our product portfolio through the identification of new-era standards-of-care therapies that work in harmony with the human gut microbiome. Our therapeutic areas of focus, incorporating the gut microbiome, include oncology and anti-infectives. We intend to expand our pipeline through our Summit Therapeutics Innovation Engine which is our research and discovery capabilities. In addition, business development activities are planned to potentially further expand our pipeline through strategic collaborations with, or acquisitions of, target opportunities that elucidate our mission.

***Clostridioides difficile* Infection Overview**

Clostridioides difficile infection (“*C. difficile* infection” or "CDI") is a bacterial infection of the colon caused by the bacterium *C. difficile* which produces toxins that cause inflammation of the colon resulting in severe watery diarrhea, painful abdominal cramping, nausea, fever and dehydration. CDI can also result in more serious disease complications, including bowel perforation, sepsis and death. CDI represents a serious healthcare issue in hospitals as the most common hospital-acquired infection, in long-term care homes and in the wider community. We estimate that there are approximately half a million cases of CDI each year across the United States based on a meta-analysis published in the Journal of Global Health in June 2019.

CDI originates from a bacterium known as *Clostridioides difficile, Clostridium difficile* or *C. difficile*. *C. difficile* sometimes can be a harmless resident of the gastrointestinal tract. The complex community of microorganisms that make up the gut microbiome usually moderates levels of *C. difficile*. The gut microbiome, which includes natural gut flora, is an essential part of the normal function of the gastrointestinal tract and also has wide implications in human health, such as the proper function of the immune system. CDI typically develops following the use of broad-spectrum antibiotic agents that can cause widespread damage to the gut microbiome and allow overgrowth of *C. difficile*. Hypervirulent *C. difficile* strains have also emerged and are frequently associated with more severe diseases. A paper published in 2018 in the peer-reviewed journal, *American Journal of Infection Control*, reported that in the United States, the hypervirulent strain, ribotype 027, accounts for approximately one-fifth of all CDI cases.

The primary clinical issue with CDI is disease recurrence. This is in contrast to other bacterial threats for which drug resistance is the principal concern. According to an article published in 2012 in the peer reviewed journal *Clinical Microbiology and Infection*, up to 25% of patients with CDI suffer a second episode of the infection. The risk of further recurrence rises to 65% after a patient suffers a third episode of CDI. In addition, each episode of recurrent disease is associated with greater disease severity and higher mortality rates. Recurrent disease is associated with an increased burden on the healthcare system.

In 2013, the CDC highlighted CDI as one of three pathogens that pose an immediate public health threat and require urgent and aggressive action. In 2019, the CDC published an updated report that continued to highlight the threat posed by CDI, with this infection classified as one of four bacterial pathogens that poses an immediate public health threat and requires urgent and aggressive action. In 2012, the Generating Antibiotics Incentives Now Act provisions of the FDA Safety and Innovation Act, or GAIN, became law. The goal of GAIN is to encourage the development of new antibiotics that treat specific pathogens, including *C. difficile*, which cause serious and life-threatening infections.

Current CDI Treatments

Existing treatment options for CDI are limited. Currently, the most commonly used treatments for CDI is vancomycin, which is a broad-spectrum antibiotic. A broad-spectrum antibiotic may not be the most appropriate treatment for CDI because although the antibiotics reduce levels of *C. difficile*, they cause significant collateral damage to the gut microbiome by killing bacteria that contribute to a healthy microbiome. This collateral damage to the gut microbiome leaves patients vulnerable to recurrent CDI. According to the Infectious Disease Society of America (“IDSA”) guidelines, the current standard-of-care for primary CDI is to treat with antibiotics, such as fidaxomicin or vancomycin. Both are recommended to treat primary CDI, and they do not have a label claim to reduce or prevent CDI recurrence. No antibiotic therapeutics are currently approved for the treatment of recurrent CDI. In October 2016, the FDA approved bezlotoxumab, a monoclonal antibody, in conjunction with an antibiotic to reduce the recurrence of CDI in patients who have a high risk of recurrence. For patients with a recurrent CDI episode within the last 6 months, IDSA suggests using bezlotoxumab as a co-intervention along with standard-of-care (SOC) antibiotics rather than SOC antibiotics alone (conditional recommendation, very low certainty of evidence). Bezlotoxumab binds to toxin B, one of the toxins produced by the *C. difficile* bacteria, to neutralize its effects. Bezlotoxumab does not treat CDI and has no direct antimicrobial activity.

Ridinilazole for the Treatment of CDI

We have been developing ridinilazole as an orally-administered, small molecule targeted antibiotic for the treatment of CDI. Ridinilazole is designed to selectively target C. difficile bacteria while preserving the microbiome and thereby treat the initial infection and reduce CDI recurrence rates. Ridinilazole is aligned with good antibiotic stewardship through its targeted spectrum of activity and the potential to reduce disease recurrence. Ridinilazole comprises of a symmetrical bis-benzimidazole scaffold which forms its core structure. We believe, based on preclinical studies conducted to date, that ridinilazole is part of a novel structural class of antibiotics that is distinct from the major classes of marketed antibiotics.

We conducted a Phase III clinical study that evaluated the benefits of ridinilazole compared to the current standard-of-care antibiotic, vancomycin, in patients with CDI. The Phase III Ri-CoDIFy trial had the primary endpoint that was testing for superiority in SCR, which is defined as Clinical Response and no recurrence of CDI within 30 days after the end of treatment. Due to the uncertainties surrounding COVID-19 and the desire of Summit to not delay the understanding of potential clinical practice-changing data, Summit combined the two trials, formerly known as “Ri-CoDIFy 1” and "Ri-CoDIFy 2,” into a single study. We refer to this Phase III clinical trial as "Ri-CoDIFy." We dosed the first patient in our Phase III clinical trials in February 2019. We enrolled 759 patients in the combined Ri-CoDIFy clinical trial.

On December 20, 2021, we announced topline results for the Phase III Ri-CoDIFy study. The study showed that ridinilazole resulted in a numerically higher SCR rate than vancomycin but did not meet the study’s primary endpoint for superiority. We will continue to evaluate the underlying data and perform additional analyses, including analyses specific to the microbiome.

In November 2015, we reported top-line results from our double blind, randomized, active controlled Phase II clinical trial that evaluated ridinilazole compared to the current standard-of-care, vancomycin, for the treatment of CDI. The Phase II clinical trial showed its primary endpoint of non-inferiority, with ridinilazole achieving statistical significance in testing the non-inferiority hypothesis to vancomycin in SCR. We subsequently reported that data from our Phase II clinical trial also showed ridinilazole to be highly preserving of the gut microbiome and secondary bile acids compared to patients who received vancomycin and experienced substantial damage to the gut microbiome, which for many patients persisted during the 30-day post-treatment period. In September 2017, we reported top-line data from our exploratory, open label, active controlled Phase II clinical trial evaluating ridinilazole compared to fidaxomicin for the treatment of CDI. In the trial, ridinilazole preserved the gut microbiome of CDI patients to a greater extent than fidaxomicin, achieving a key secondary endpoint. The overall safety profile of ridinilazole remains unchanged.

Ridinilazole Clinical Development

Phase III Clinical Trial Program

In the Ri-CoDIFy trial, we randomized patients in a one-to-one ratio to receive either a 200 mg dose of ridinilazole tetrahydrate administered twice per day for ten days or a 125 mg dose of vancomycin administered four times per day for ten days. Due to the different treatment regimens, we developed dummy placebos that are administered to the patients in the Phase III clinical trials according to a schedule designed to maintain the blind within each trial. Enrolled patients in Ri-CoDIFy were required to be at least 18 years of age or older, have a confirmed diagnosis of CDI as measured by the presence of toxin A and/or toxin B of *C. difficile* in the stool as confirmed by a positive free toxin test, and must not have had more than one prior episode of CDI in the previous three months, or more than three episodes in the prior 12 months.

The Ri-CoDIFy Phase III clinical trial was designed to assess, as its primary endpoint, the superiority of ridinilazole compared to vancomycin in Sustained Clinical Response, or SCR, which was defined as Clinical Response of the treated episode of CDI and no recurrence of CDI through 30 days after the end of treatment. Additional endpoints included Clinical Response ("CR"), recurrence rate, safety and tolerability, analyses of the gut microbiome and metabolome, in addition to quality of life and health economic outcome measures.

On December 20, 2021, we announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole for the treatment of and Sustained Clinical Response for patients suffering from *C. difficile* infection. The study showed that ridinilazole resulted in a numerically higher SCR rate than vancomycin but did not meet the study's primary endpoint for superiority. We will continue to evaluate the underlying data, including analyses specific to the microbiome.

Phase II Clinical Trial in Patients with CDI

In November 2015, we reported top-line results from our randomized, double blind, active controlled, multicenter, Phase II clinical trial of ridinilazole in patients with CDI, and we subsequently presented additional data. We referred to this as our Phase II proof of concept clinical trial and as the "CoDIFy" study.

We conducted this clinical trial at approximately 35 sites in the United States and Canada. The trial was conducted under an Investigational New Drug Application, or IND, that we submitted to the FDA in January 2014. We enrolled a total of 100 patients between 18 to 90 years of age. The trial randomized patients in a one-to-one ratio to receive either a 200 mg dose of ridinilazole tetrahydrate administered twice per day for ten days or a 125 mg dose of vancomycin administered four times per day for ten days.

The primary objective of this clinical trial was to evaluate the efficacy of ten days of dosing with ridinilazole compared to treatment with vancomycin. The primary efficacy endpoint was non-inferiority on sustained clinical response, or SCR, which was defined as clinical cure based on the resolution of diarrhea at the test of cure, or TOC, visit on day 12 and no recurrence of CDI within 30 days after the end of treatment. The secondary efficacy endpoints were investigator assessed clinical response at the TOC visit and rate of recurrence of CDI within 30 days after the end of treatment. Secondary objectives of this clinical trial were the assessment of the safety and tolerability of ten days of dosing of ridinilazole compared to vancomycin, the plasma and fecal concentrations of ridinilazole in patients with CDI who received ridinilazole and the health status of CDI patients who received ten days of treatment of ridinilazole compared to patients who received ten days of treatment of vancomycin. We also assessed the impact of vancomycin or ridinilazole on the gut microbiome of patients in the clinical trial as one of a number of exploratory objectives.

Analysis of Results

We observed the following results in our Phase II proof of concept trial:

- ***Ridinilazole Demonstrated Statistical Superiority Over Vancomycin for the Primary Endpoint.*** Our Phase II proof of concept trial met its primary endpoint with ridinilazole achieving a SCR rate of 66.7% compared to 42.4% for vancomycin (non-inferiority margin of 15%, p=0.0004 for testing non-inferiority). At the pre-specified 2-sided alpha level of 0.10, ridinilazole was statistically superior to vancomycin. The primary analysis was conducted on the modified intent-to-treat, or mITT, population (36 patients dosed with ridinilazole, 33 patients dosed with vancomycin) that comprised patients with CDI confirmed by the presence of free toxin in feces. We also observed a generally consistent trend of improved SCR with ridinilazole across subgroups at higher risk of recurrence, including the elderly, patients who were on concomitant antibiotics at the start of treatment and patients with a prior history of CDI.

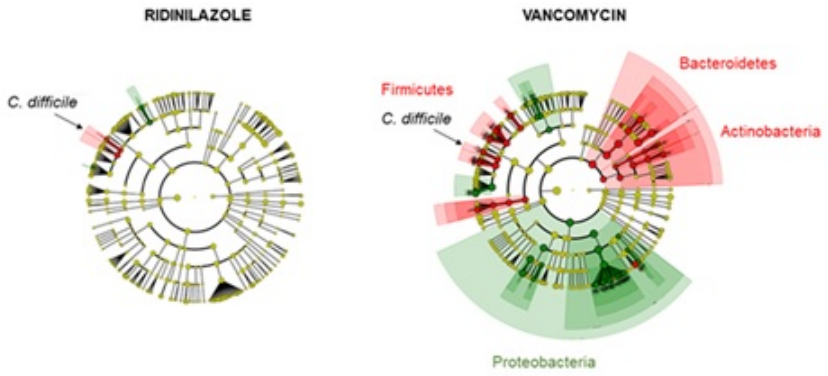
- ***Ridinilazole Demonstrated a Large Reduction in Rates of Recurrence Compared to Vancomycin.*** We observed that the statistical superiority at 2-sided alpha of 0.10 (which was prespecified in the protocol) in SCR with ridinilazole compared to vancomycin was driven by a large numerical reduction in rates of disease recurrence. Clinical cure rates at the end of ten days of treatment were similar, with ridinilazole achieving a rate of 77.8% compared to 69.7% for

vancomycin, but ridinilazole achieved a recurrence rate of 14.3% compared to 34.8% for vancomycin during the 30-day post-treatment period.

- ***Ridinilazole had Minimal Impact on the Gut Microbiome.*** The microbiome primary analysis of the Phase II study was performed on fecal samples collected from CDI patients at baseline, and at end of therapy (EOT, Day 10). This analysis showed that ridinilazole had minimal impact on the gut microbiome diversity and composition compared to vancomycin indicating a smaller impact on microbiota health and preservation of resistance to infections. No or minimal loss in alpha-diversity was observed following 10 days treatment with ridinilazole, whereas a significant loss in diversity was observed with vancomycin. Ridinilazole also showed minimal impact on the gut microbiome composition with significant reductions in relative abundance limited to only a few taxa from the Firmicutes: 36-fold reduction of the Peptostreptococcaceae family that contains *C. difficil*e, and 15-fold and 10-fold reductions of the Ruminococacceae and Clostridiaceae, respectively. In contrast, vancomycin resulted in significant reductions in the relative abundance of several families in the Firmicutes (e.g. >1000-fold for Lachnospiraceae and >500-fold for Ruminococcaceae), in the Bacteroidetes (>1000- fold) and in the Actinobacteria (5-fold) phyla. These impacts are demonstrated in the illustraiont below. These reductions were associated with a >20-fold increase in the Proteobacteria and, in particular, a >200-fold increase in Enterobacteriaceae and >1000-fold increase in *Klebsiella spp*. This further gut dysbiosis with the expansion of Enterobacteriaceae pathogens may put patients at risk for subsequent infections, including multi-drug resistant pathogens such as the carbapenem-resistant *K. pneumoniae*.

Differential impact of ridinilazole and vancomycin on the gut microbiota

Changes in relative abundance of bacterial taxa in CDI patients after 10 day-treatment with ridinilazole or vancomycin

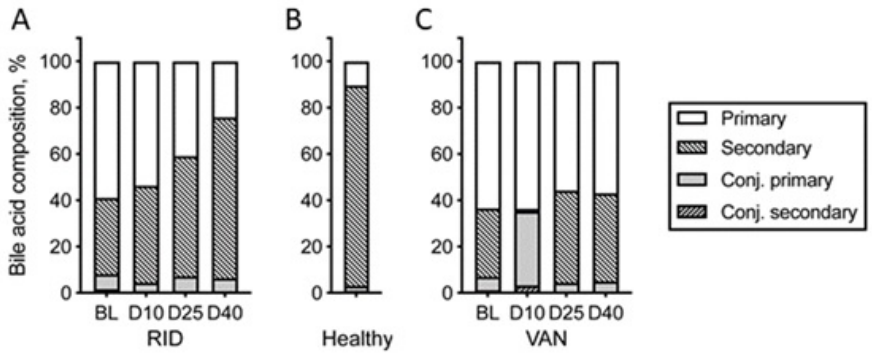


Red: lower abundance at the end of treatment Green: higher abundance at the end of treatment

- ***Ridinilazole Preserved the Gut Bile Acid Composition.*** Bile acids are metabolized by bacteria within the gut. These bile acids exist in different forms that can either favor or block the growth of *C. difficile*. As expected, in healthy controls, bile acids that can block *C. difficile* growth, i.e., the protective bile acids were predominant while in Phase II CDI patients bile acids that can promote *C. difficile* growth were predominant. Ridinilazole treatment preserved the gut bile acid composition and allowed a gradual normalization post-treatment. At 30 days post-EOT, the bile acid composition of ridinilazole-treated patients trended towards that of healthy subjects showing a predominance of the protective bile acids. In contrast, vancomycin treatment resulted in further alteration of the bile acid composition and a significant decrease of the protective bile acids to < 1% of the total bile acids at EOT. At 30 days post-EOT, their bile acid profile was similar to that observed in the CDI patients prior to therapy, potentially predisposing vancomycin- treated patients to recurrence of the infection.

Differential impact of ridinilazole and vancomycin on gut bile acids

Fecal bile acid composition in healthy control subjects,
ridinilazole- and vancomycin-treated subjects



BL: baseline; conj: conjugated; D10: Day 10, end-of-treatment; D25: Day 25; D40: Day 40 or 30 days post-EOT

- ***Ridinilazole was Retained in the Gastrointestinal Tract.*** Ridinilazole was restricted to the gastrointestinal tract, which is the site where CDI occurs in the body. Systemic exposure was close to or below the level of detection in patients with CDI, with plasma concentrations very similar to those observed in our Phase I clinical trial in healthy volunteers.

- ***Ridinilazole Reduced Biomarkers of Inflammation.*** We measured levels of two key markers of inflammation, calprotectin and lactoferrin, in feces collected from the 69 patients who comprised the mITT group. The samples analyzed were collected at the time of randomization (prior to initiation of treatment), at day five and at day ten. We observed that ridinilazole and vancomycin reduced concentrations of calprotectin and lactoferrin by similar levels when analyzing the results for all patients. We also observed that a subset of patients with severe CDI had a greater reduction in levels of calprotectin and lactoferrin when treated with ridinilazole compared to vancomycin. We believe these data indicate that ridinilazole is associated with a greater reduction in inflammatory markers compared to vancomycin in patients with severe CDI.

- ***Ridinilazole Significantly Improved Short- and Longer-Term Quality of Life Measures.*** Patients completed the EuroQol 5-Dimension questionnaire (three level version; EQ-5D-3L) at baseline, day 5, day 10, day 12 and day 40 to assess the impact of treatment with ridinilazole and vancomycin on five dimensions of physical and mental health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. As early as day 5, ridinilazole-treated patients reported improvements in index scores ($p=0.008$), a measure that combines scores from the five domains and visual analogue scale, or VAS, scores ($p=0.01$), which is a self-reported score of overall health. More specifically, by day 40, patients treated with ridinilazole had improved significantly more than patients treated with vancomycin in anxiety and depression measures. In addition, while both treatment arms showed significant improvements in pain and discomfort with treatment, by day 10, fewer patients treated with ridinilazole reported issues than did those treated with vancomycin. We believe these findings support the potential for the benefits of treatment with ridinilazole to extend beyond clinical benefits to the overall wellbeing of the patient.

- ***Ridinilazole was Well Tolerated.*** Ridinilazole was generally well tolerated. The overall rate of adverse events and serious adverse events reported in the ridinilazole and vancomycin treatment arms were comparable.

Phase II Exploratory Clinical Trial of Ridinilazole Compared to Fidaxomicin

In September 2017, we reported top-line data from our randomized, open label, active controlled, multicenter Phase II clinical trial evaluating ridinilazole compared to fidaxomicin for the treatment of CDI. This exploratory clinical trial was designed to generate data comparing ridinilazole to fidaxomicin, a CDI antibiotic launched in 2011, and the results of this clinical trial are expected to help to inform the commercial positioning of ridinilazole. We conducted this clinical trial at sites in the United Kingdom, Europe and the United States, enrolling 27 patients between 18 and 90 years of age. We randomized patients in a one-to-one ratio to receive either a 200 mg dose of ridinilazole tetrahydrate administered twice per day for ten days or a 200 mg dose of fidaxomicin administered twice per day for ten days. The trial population was unbalanced with more patients randomized to ridinilazole having predisposing factors for recurrent CDI, and at a higher risk of poorer clinical outcomes as measured by ATLAS score, a tool for evaluating CDI in patients by age, temperature, leukocytes and albumin levels, and use of systemic antibiotics.

The primary efficacy objective of this clinical trial was to determine the safety and tolerability of ten days of dosing with 200 mg BID of ridinilazole tetrahydrate compared to dosing with 200 mg BID of fidaxomicin. The secondary objectives of the clinical trial were to assess the following:

- the plasma pharmacokinetics of ridinilazole in patients with CDI;

- the qualitative and quantitative effect of ridinilazole and fidaxomicin on the gut microbiome;
- the plasma, urine and fecal concentrations of ridinilazole and its metabolites; and
- the efficacy of ten days of dosing with ridinilazole compared to fidaxomicin for the treatment of CDI.

The measurement of efficacy was based on investigator assessed clinical response at the test of cure, or TOC, visit, with clinical cure defined as resolution of diarrhea while on treatment and maintained at the TOC visit, and sustained clinical response, defined as clinical cure at the TOC visit and no recurrence of CDI within 30 days after the end of treatment.

We reported the following findings:

- ***Ridinilazole Preserved the Microbiome to a Greater Extent than Fidaxomicin.*** We observed that the ten days treatment with ridinilazole had markedly less of an impact on the gut microbiome of trial patients by measures of overall diversity and changes in key bacterial groups when compared to those trial patients dosed with fidaxomicin. We observed that while ridinilazole and fidaxomicin both reduced the abundance of *C. difficile*, fidaxomicin treated patients had reduced abundance of other bacterial families, including the Ruminococcaceae family from the Firmicutes, that are thought to have direct functional roles in protecting against CDI. We observed that for a number of these bacterial families, the difference between the two treatments reached statistical significance. We also reported alpha diversity, as measured by the Simpson's Diversity Index, as another measure of microbiome health. We observed a greater reduction in alpha-diversity during fidaxomicin treatment compared with ridinilazole treatment. These measures were a key secondary endpoint of the trial. We believe that these measures provide further evidence of ridinilazole's precision in killing *C. difficile* while preserving the gut.

- ***Ridinilazole was Well Tolerated.*** The primary endpoint of the trial was safety, as measured by the number of treatment emergent adverse events and serious adverse events. During the trial, no new or unexpected safety signals were identified and ridinilazole was well tolerated.

- ***Comparable Rates of Sustained Clinical Response.*** We observed that seven of the 14 ridinilazole-treated patients and six of the 13 fidaxomicin-treated patients were cured at the end of treatment and did not have a recurrence of CDI within the following 30 days to achieve a sustained clinical response. The trial was however not designed for efficacy comparisons due to the small number of patients enrolled, and so we believe no conclusions on efficacy should be made based solely on these data.

Phase I Clinical Trial in Healthy Volunteers

In 2013, we completed a randomized, partially blind, placebo-controlled Phase I clinical trial of ridinilazole in healthy volunteers. We conducted this clinical trial at a single site in the United Kingdom under approval from the U.K. Medicines and Healthcare products Regulatory Agency, or MHRA, and the Ethics Review Committee. We enrolled 56 healthy male subjects in the clinical trial who were between 18 and 55 years of age. The primary objective of the clinical trial was to determine the safety and tolerability of single and multiple ascending oral doses of ridinilazole. The secondary objectives included determining the single and multiple oral dose pharmacokinetics of ridinilazole, assessing the effect of food on systemic exposure of ridinilazole and assessing the effect of multiple oral doses of ridinilazole on gut flora.

We conducted the clinical trial in two parts. Part 1 consisted of an ascending single dose study and a food effect evaluation study. In Part 1, we evaluated a total of 40 subjects, divided into the following six cohorts:

- four fasted subjects, randomized for three subjects to receive a single 2 mg dose of ridinilazole and one subject to receive placebo;
- four fasted subjects, randomized for three subjects to receive a single 20 mg dose of ridinilazole and one subject to receive placebo;
- eight fasted subjects, randomized for six subjects to receive a single 100 mg dose of ridinilazole and two subjects to receive placebo;
- eight fasted subjects, randomized for six subjects to receive a single 400 mg dose of ridinilazole and two subjects to receive placebo;
- eight fasted subjects, randomized for six subjects to receive a single 2,000 mg dose of ridinilazole and two subjects to receive placebo; and

- eight subjects, randomized for six subjects to receive a single 1,000 mg dose of ridinilazole under fasted conditions and a single 1,000 mg dose under fed conditions, and two subjects to receive two single doses of placebo on the same dosing schedule. The doses under fed and fasted conditions were separated by a minimum of six days.

Part 2 of the clinical trial consisted of a multiple dose study. In Part 2, we evaluated a total of 16 subjects, who were divided into the following two cohorts:

- eight subjects randomized for six subjects to receive 200 mg doses of ridinilazole twice per day for nine days with a single final dose on day ten and two subjects to receive placebo on the same dosing schedule; and

- eight subjects randomized for six subjects to receive 500 mg doses of ridinilazole twice per day for nine days with a single final dose on day ten and two subjects to receive placebo on the same dosing schedule.

Analysis of Trial Results

We observed the following results in this clinical trial:

- ***Ridinilazole was Well Tolerated.*** Ridinilazole was well tolerated at all doses tested in the clinical trial. The incidence of adverse events in the clinical trial was low for patients treated with ridinilazole and comparable to the incidence of adverse events for patients receiving placebo. The majority of the adverse events that were considered to be possibly related to ridinilazole were classified as gastrointestinal disorders and were mild in severity and resolved without intervention. One patient withdrew from the clinical trial after suffering from appendicitis on day one. The trial investigator determined this serious adverse event was unlikely to be related to treatment with ridinilazole.

- ***Ridinilazole was Retained in the Gastrointestinal Tract.*** Ridinilazole was targeted to the gastrointestinal tract, which is the site where CDI occurs in the body. Systemic exposure was close to or below the level of detection in both fed and fasted subjects.

- ***Ridinilazole was Highly Selective for Total Clostridia Bacteria with Minimal Impact on Other Natural Gut Flora.*** We measured levels of bacteria in fecal samples from Part 2 of the clinical trial for gut microbiome composition on the day prior to commencement of dosing and on days four and nine of the 10-day treatment. In both the 200 mg BID and 500 mg BID dose cohorts, median levels of key bacteria groups that comprise the natural gut microbiome remained relatively constant during this period and did not fluctuate substantially from baseline. The one exception was the total clostridia bacterial group which decreased from the baseline level to zero by day four of dosing and remained at zero on day nine of dosing. We did not detect any *C. difficile* viable cells or spores in the fecal samples of any of the healthy volunteer subjects at any point during the clinical trial. Thus, ridinilazole affected the count of clostridia other than *C. difficile* but not of any other bacteria groups that comprise the gut microbiome.

CDI Preclinical Data

In a range of preclinical studies, ridinilazole demonstrated an encouraging profile as a potential antibiotic for the treatment of initial CDI and reduction of CDI recurrence. The following is a summary of key observations from these studies:

- ***Potency Against C. difficile***. We screened the *in vitro* activity of ridinilazole and a range of different comparators including fidaxomicin, metronidazole and vancomycin against nearly 700 *C. difficile* clinical isolates. Clinical isolates have been collected in Europe, U.S. and Asia-Pacific and included a range of ribotypes including the hypervirulent ribotype RT 027 and most common ribotypes in Europe and U.S. In these studies, ridinilazole was highly potent against all *C. difficile* clinical isolates, either equally potent to, or more potent than, fidaxomicin and more potent than both vancomycin and metronidazole. Ridinilazole did not display evidence of cross resistance with other classes of key antibiotics in common use.

- ***Targeted Spectrum of Activity***. We conducted *in vitro* testing of ridinilazole, vancomycin, metronidazole and fidaxomicin against a wide panel of bacteria that are commonly found in the gut microbiome and are necessary for normal function of the gastrointestinal tract and also have wide implications on human health, such as the proper function of the immune system. As illustrated in the figure below, in this study ridinilazole had minimal activity against these beneficial bacterial groups. Ridinilazole also displayed higher selectivity for *C. difficile* in this study as compared to vancomycin, metronidazole and fidaxomicin. *In vitro* potency is measured by determining the concentration of a drug (in micrograms per milliliter) needed to inhibit the growth of 90% of the bacterial strains being tested, referred to as a MIC90 measurement. A high number, typically higher than 256, indicates a weak antimicrobial effect, and a low number, typically less than eight, indicates a potent antimicrobial effect. We believe that the targeted spectrum of activity for ridinilazole seen in this study compared to the relatively broad-spectrum of activity of other antibiotics indicates the potential for ridinilazole to selectively target *C. difficile* bacteria while preserving the microbiome and thereby reduce CDI recurrence rates.

Profile of Selectivity of Ridinilazole vs. Other CDI Antibiotics

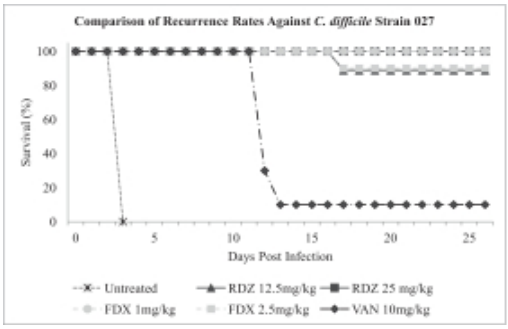
Key Bacterial Groups	Spectrum of Activity – MIC_{90} (μg/mL)			
	RDZ	MTZ	VAN	FDX
Bacteroides spp.	>512	2	128	>512
Bifidobacterium spp.	>512	128	1	0.125
Lactobacillus spp.	>512	>512	>512	>512
Eggerthella lenta	>512	0.5	4	≤0.03
Peptostreptococcus spp.	64	1	0.5	≤0.03
Staphylococcus aureus	>512	>512	1	16

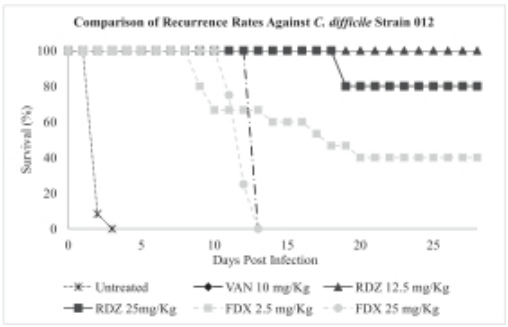
Antibiotic effect: Weak; Medium; Potent

RDZ: Ridinilazole VAN: Vancomycin
MTZ: Metronidazole FDX: Fidaxomicin

- ***Novel Mechanism of Action (MOA)***. Ridinilazole is believed to drive its bactericidal effect through a novel MoA that results in lethal perturbation of cell division. We have conducted further studies to characterize the MoA. It has now been demonstrated that ridinilizole is able to bind, with high affinity, to the minor groove of double-stranded DNA substrates, including *C. difficile* genomic DNA. Cell imaging using fluorescence confocal microscopy has revealed that ridinilazole exclusively co-localizes with genomic DNA in *C. difficile.* DNA binding is believed to be the primary mechanism through which ridinilazole exerts its bactericidal activity in *C. difficile*. Further studies will be conducted to determine the biological consequences of ridinilazole binding to genomic DNA in *C. difficile*.

- ***Protection Against CDI Recurrence***. In a hamster model, we infected one group of hamsters with a *C. difficile* strain from the hypervirulent ribotype 027 and a second group of hamsters with the *C. difficile* virulent reference strain 630, ribotype 012. Hamsters from each group were treated for 5 days with different doses of ridinilazole, vancomycin and fidaxomicin and recurrence of the infection was evaluated over the 21 days following treatment. In this hamster model, a hamster fatality within the first five days is a result of initial *C. difficile* infection, while a fatality from day six to day 25 is a result of recurrent disease. As illustrated in the figure below, the hamsters treated with two different doses of ridinilazole had survival rates of 90% to 100% against strain ribotype 027 and 80% to 100% against strain ribotype 012. These survival rates were higher than hamsters treated with vancomycin (0% to 10% survival rates) for both CDI strains, comparable to hamsters treated with two different doses of fidaxomicin against strain ribotype 027 (90% to 100% survival rates) and higher than hamsters treated with two different doses of fidaxomicin against strain ribotype 012 (0% to 40% survival rates). All infection control hamsters received placebo and died by the second day following infection.





- ***Ridinilazole Arrests Cell Division.*** In *in vitro* studies, treatment of *C. difficile* bacteria prevented bacterial replication, eventually resulting in death of the bacterial cells. We have also observed significant increases in the length of *C. difficile* cells and an absence of division septum formation, suggesting replication is halted by prevention of bacterial division.

- ***Inhibition of Sporulation.*** *C. difficile* can form spores – a dormant, protected form of the bacterium which contributes to infection recurrence, is highly resistant to standard cleaning practices and leads to environmental persistence and disease transmission. During *in vitro* studies, we found that treatment of *C. difficile* with ridinilazole at concentrations which prevent bacterial replication also prevents sporulation. We believe that inhibition of sporulation may help reduce the incidence of recurrent disease.

- ***Reduction in Toxin Levels in vitro.*** *C. difficile* produces toxins A and B to elicit an inflammatory response in the host, resulting in the symptoms of the disease including severe diarrhea. We found during *in vitro* studies that treatment of *C. difficile* with ridinilazole at concentrations which prevent bacterial replication reduce toxin A and B production.

- ***Low Propensity for Resistance.*** *In vitro* studies exposing *C. difficile* to ridinilazole have shown that the frequency of spontaneous resistance to ridinilazole is low. Resistant mutants that do arise, or are forcefully selected for by passaging in the presence of sub-inhibitory levels of ridinilazole, importantly showed no cross-resistance to other standard-of- care antibiotics.

- ***Concomitant Antibiotic Use.*** In an *in vitro* bacterial culture study, we exposed *C. difficile* to ridinilazole in combination with selected other antibiotics. In this study, concomitant use of antibiotics had neither a synergistic nor an antagonistic effect on the minimal inhibitory concentration of ridinilazole, with the exception of lincosamide antibiotics (clindamycin and lincomycin). For these compounds, an additive (nearly synergistic) interaction was observed. We believe these results indicate that concomitant use of other antibiotics will not diminish the potency of ridinilazole. This is an important finding because a significant portion of CDI patients receive antibiotic treatment for persistent or new infections.

Other Pipeline Product Candidates

Discuva Platform

Our Discuva Platform is a genetics-based technology that can be used throughout the stages of drug discovery from hit-to-lead through candidate selection. Our Discuva Platform aligns modified bacterial transposon mutagenesis with next generation sequencing and a proprietary end user interface.

The Discuva Platform uses pathogen specific transposons. Transposons are small segments of DNA that are capable of replicating and inserting copies of DNA at random sites in the same or a different chromosome. Our pathogen specific transposons have three different activating promoters to drive bacterial gene upregulation, to cause gene disruption, or cause the downregulation of bacterial gene expression. There is a single transposon insertion per genome. The density of transposon insertion at the different genomic loci is determined in the whole library with insertion rates potentially being as high as every two to three base pairs.

We believe that our Discuva Platform has three principal uses:

i) Identifying Essential Genes in Bacteria. We are able to use our Discuva Platform to identify genes within bacteria that are essential for their survival. This allows us to identify new bacterial targets against which to develop new antibiotic drugs.

ii) Elucidating Mechanism of Action. We are able to use our Discuva Platform to elucidate the mechanism of action of a compound to be inferred by the genes that are upregulated during experiments when in the presence of a drug. We are able to rapidly identify the mechanism of action of a potential drug and this represents an important capability of our Discuva Platform. We have been able to validate the ability of our Discuva Platform to elucidate mechanisms of action by testing antibiotic compounds representative of known classes whose mechanisms of action are known.

iii) Understanding Emergent Mechanisms of Resistance. We are able to use our Discuva Platform to test a compound's susceptibility towards known mechanisms of antibiotic resistance to allow us to select potential drug candidates with what we believe will be much better resistance profiles. We believe the importance of understanding patients prior to the development of widespread resistance.

Enterobacteriaceae Program

We are developing a new mechanism novel small molecule antibiotic (SMT-738 which has originated from our DDS-04 series) for the potential treatment of infections caused by the Enterobacteriaceae, a family of Gram-negative bacteria which includes *E. coli* and *Klebsiella* species. Enterobacteriaceae are responsible for causing serious infections across multiple indications, for example bloodstream infections, urinary tract infections and hospital-acquired pneumonias. Multi-Drug Resistant ("MDR") Enterobacteriaceae are resistant to treatment by most or occasionally all existing classes of known antibiotics. The most difficult to treat infections are those caused by the Extended Spectrum Beta-Lactamase ("ESBL")-producing Enterobacteriaceae and the Carbapenem-resistant Enterobacteriaceae ("CRE"). According to the CDC, ESBL-producing and CRE Enterobacteriaceae have collectively caused an estimated 197,400 infections and 9,100 deaths in hospitalized patients in the United States in 2019.

We identified the novel DDS-04 series using our Discuva Platform and, like ridinilazole, the DDS-04 series has a targeted- spectrum of activity, in this case highly specific for Enterobacteriaceae. The DDS-04 series act *via* a clinically unexploited target, LolCDE, which is involved in the transport of lipoproteins from the inner to outer membrane in Gram-negative bacteria. The cell membrane is crucial for cell viability and the *lol* genes are essential in bacteria such as *E.coli*. In April 2019, we

reported data that showed our DDS-04 series to be rapidly bactericidal and highly potent across globally diverse Enterobacteriaceae strains, including multi-drug resistant isolates. Importantly, our DDS-04 series has a low propensity for resistance development and displays no cross resistance with existing classes of antibiotics. In July 2019, we reported initial, positive proof of concept data on an exemplar compound from our DDS-04 series across *in vivo* rodent models of sepsis, urinary tract infection, and pneumonia with further data presented in September 2019.

On May 18, 2021, we announced SMT026738 ("SMT-738") as our preclinical candidate to combat multidrug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. SMT-738 is the first of a novel class of precision antibiotics. Combining a novel antibiotic class (SMT-738) with a clinically unexploited target (LolCDE) mitigates the risk of pre-existing resistance, potentially allowing for the effective treatment of infections caused by Enterobacteriaceae that currently have very limited and failing treatment options due to resistance to existing antibiotic classes.

We retain worldwide clinical development and commercial rights to SMT-738. We have been and plan to continue to perform IND-enabling activities.

Our Collaborations and Funding Arrangements

BARDA

In September 2017, we were awarded a contract from the Biomedical Advanced Research and Development Authority, or BARDA, to fund, in part, the clinical and regulatory development of ridinilazole for the treatment of infections caused by *C. difficile*. The contract includes a base period with federal government funding of approximately $32.0 million. In addition, there are three option work segments that, if exercised in full by BARDA, would increase the total federal government funding under the contract to approximately $62.0 million. In August 2018, BARDA exercised one of the option work segments worth $12 million. In June 2019, BARDA increased the total value of the funding contract to up to $63.7 million and also exercised a second option work segment worth $9.6 million. In January 2020, BARDA increased the contract by a further $8.8 million.

This increased the total value of the funding contract to $72.5 million and brought the total amount of committed BARDA funding to $62.4 million. The remaining federal government funding is dependent on BARDA in its sole discretion exercising the final independent option work segment, upon the achievement by the Company of certain agreed-upon milestones for ridinilazole. As of December 31, 2021, an aggregate of $56.5 million of the total committed BARDA funding has been received and the Company has recognized $50.3 million of cumulative income since contract inception. The contract provides for a cost-sharing arrangement under which BARDA funds a specified portion of estimated costs for the continued clinical and regulatory development of ridinilazole for CDI. Under this cost sharing arrangement, we are responsible for a portion of the costs associated with each segment of work, including any costs in excess of the estimated amounts.

During the base period of the contract, BARDA agreed to fund, in part, activities for our two Phase III clinical trials of ridinilazole, which were later combined into one trial (Ri-CoDIFy), and included obtaining requisite regulatory approvals for the opening of trial sites, arranging for the manufacture of clinical supply of ridinilazole and engaging third-party contract research organizations to conduct the clinical trials including initial patient enrollment and treatment. Under the original terms of the award, the three option work segments, if exercised in full, provided for up to an additional $30 million of funding from BARDA to support the development of ridinilazole through to potential submission of applications for marketing approval. As described above, the award was amended twice, bringing the total of additional funding available beyond the base period to $40.5 million. In August 2018, one of the three option work segments was exercised by BARDA with the $12.0 million in funding to be drawn down to specifically support drug manufacturing activities required for the submission of marketing approval applications and other regulatory activities. In June 2019, a second of the three option work segments was exercised by BARDA with the $9.6 million in funding to be drawn down to support patient enrollment and dosing in the Phase III clinical trials of ridinilazole. In January 2020, BARDA increased its award by $8.8 million, with this additional funding to support a new clinical trial in adolescent patients. Activities to be covered by the remaining option work segment include the preparation, submission and review of applications for marketing approvals of ridinilazole for CDI in the United States.

The remaining option work segment is an independent, discrete work segment that is eligible to be exercised, in BARDA's sole discretion, upon the completion of agreed-upon milestones and deliverables. If this option work segment is exercised by BARDA, the contract will run through April 2022, unless extended by us and BARDA.

The contract specifies the plan of activities to be conducted under the contract. In addition to our obligations to conduct the activities provided for by the plan, we are obligated to satisfy various federal reporting requirements, addressing clinical progress, technical issues, and intellectual property and financial matters. Payments to us under the contract are expected to be made monthly after we invoice BARDA for allowable costs that have been incurred.

BARDA may terminate this agreement upon our uncured default in our performance of the agreement or at any time if the contracting officer determines that it is in the U.S. government's interest to terminate the agreement.

Under standard U.S. government contracting terms, the U.S. government receives only limited rights for government use of certain of our pre-existing data and certain data produced with non-federal funding, to the extent such data are required for delivery to BARDA under the contract. The U.S. government receives unlimited rights to use and disclose new data first produced under the contract with BARDA. Except for commercialization rights to ridinilazole in South America, Central America and the Caribbean, we currently have exclusive worldwide commercialization rights to ridinilazole and retain these rights under the BARDA contract. However, the U.S. government is entitled to a nonexclusive, nontransferable, worldwide, royalty-free license to practice or have practiced any patent on an invention that is conceived or first reduced to practice under the contract, which is referred to as a subject invention.

In addition, the U.S. government may obtain additional rights if we do not elect to retain ownership of a subject invention or if we do not satisfy certain disclosure and patent prosecution obligations with respect to a subject invention. Furthermore, the government is entitled to march-in rights under our contract with BARDA. March-in rights permit the U.S. government to require that we grant a license to a subject invention to a third party if we have not taken effective steps to achieve practical application of the invention within a reasonable time; if such action is necessary to meet health and safety needs and/or requirements for public use that we are not meeting; or if we have not obtained from any exclusive licensee the required agreement for manufacturing such invention substantially in the United States or a waiver of this requirement.

Wellcome Trust

In October 2012, we entered into a translation award funding agreement with the Wellcome Trust Limited, as trustee of the Wellcome Trust, in order to support a Phase I and a Phase II clinical trial of ridinilazole for the treatment of CDI. We refer to the translation award funding agreement as the translation award agreement. Under the translation award agreement, we were eligible to receive up to $6.3 million from the Wellcome Trust, of which we received the entire $6.3 million. The translation award agreement followed a funding agreement we and the Wellcome Trust entered in October 2009, which we refer to as the discovery award agreement, under which we received $3.7 million for preclinical development of CDI antibiotics. We refer to any compound or product that is covered by intellectual property rights created under the discovery award agreement or the translation award agreement, or that is covered by intellectual property rights that we created or to which we had rights prior to October 2009 and that relate to the activities under the discovery award agreement or the translation award agreement, as the award products. We agreed to use commercially reasonable efforts to achieve certain development milestones by specified dates.

We would be required to make a full or partial repayment to the Wellcome Trust of the funding we received under the translation award agreement, plus accrued interest, under specified conditions, including our unauthorized use of the award amount, our fraudulent or willful misconduct, our knowingly withholding material information from the Wellcome Trust, or an acquisition by certain third parties of all or a material part of our business or assets or of a majority of our equity. Upon such a full repayment, our obligation to share a portion of net revenue with the Wellcome Trust would terminate.

Termination

Unless earlier terminated by the Wellcome Trust, the translation award agreement will terminate on the earlier of our full repayment of the award amount, plus accrued interest, to the Wellcome Trust following its request for repayment, or the expiration of all payment obligations under the translation award agreement and the revenue sharing agreement. The Wellcome Trust may terminate the translation award agreement for specified reasons, including our material breach or insolvency related events or the Wellcome Trust's determination that the clinical trials should be terminated due to a serious failure in the progress, management or conduct of the clinical trials, if we do not remedy such condition within a specified period after receiving notice.

Assignment

We may not, without the Wellcome Trust's prior consent, assign, transfer or declare a trust over the translation award agreement or otherwise dispose of any of our rights or obligations under the translation award agreement, with such consent not being unreasonably withheld, delayed or conditioned, other than an assignment to our affiliates.

Revenue Sharing Agreement

The terms of the translation award agreement required us to enter into a revenue sharing agreement with the Wellcome Trust prior to the further development (beyond the Phase II trial supported by the 2012 translational award agreement) and commercialization, which together we refer to as the "Exploitation" of any compound or product that is covered by the intellectual property rights created under the translational award agreement or the discovery award agreement, or that is covered by background intellectual property rights. Under such revenue sharing agreement, the Wellcome Trust would be entitled to a share of the net revenue that we, our affiliates, licensees or third-party collaborators receive under the Exploitation of the award products or any intellectual property associated with such Exploitation.

In October 2017, we entered into a revenue sharing agreement with the Wellcome Trust. Under the terms of the revenue sharing agreement: (i) if we commercialize ridinilazole, the Wellcome Trust is eligible to receive a low-single digit percentage of net revenue (as defined in the translation award agreement), and a one-time milestone payment of a specified amount if cumulative net revenues exceed a specified amount; (ii) if a third party commercializes ridinilazole, the Wellcome Trust is eligible to receive a mid-single digit percentage of the net revenues we receive from commercial sales by such third party, and a one-time milestone payment of a specified amount if cumulative net revenues we receive exceed a specified amount. In addition, following the first commercial sale by such third party, the Wellcome Trust is eligible to receive a one-time milestone payment equal to a low-single digit percentage of the aggregate amount of any pre-commercial payments we receive from third-party licensees prior to such commercial sale; and (iii) in the event of an assignment or sale of the assets or intellectual property pertaining to ridinilazole, the net proceeds we receive from such assignment or sale would be treated as net revenue under the revenue sharing agreement.

Under the revenue sharing agreement, it was agreed that any development funding or grant funding we receive from BARDA or other third parties, including licensees, would not be classified as net revenue or as a pre-commercial payment. In addition, under the revenue sharing agreement, the Wellcome Trust agreed to terminate all of its rights under the translation award agreement to develop or commercialize the award products or the related intellectual property in specified markets and in
specified indications, in the event that we were not developing or commercializing the award products or such intellectual property for such markets or in such indications.

Unless earlier terminated, the revenue sharing agreement will expire upon the later of the expiration of the last patent or patent application covering ridinilazole; the expiration of any agreement or payment obligations that we have entered into with a third party relating to the Exploitation of ridinilazole; or the expiration of any payment obligations owed to the Wellcome Trust relating to the Exploitation of ridinilazole. In addition, each party has the right to terminate the revenue sharing agreement if the other party materially breaches the agreement, and the breach remains uncured for a specified period or the breach is uncurable, or if the other party experiences specified insolvency related events.

Eurofarma Laboratórios S.A.

In December 2017, we entered into an exclusive license and commercialization agreement with Eurofarma, pursuant to which we granted Eurofarma the exclusive right to commercialize ridinilazole in Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Dominican Republic, Uruguay and Venezuela, which we refer to as the licensed territory. We have retained commercialization rights in the rest of the world.

Financial Terms

Under the terms of the license agreement, we received an upfront payment of $2.5 million and are entitled to receive additional development milestones upon the achievement of staged patient enrollment targets in the licensed territory in our Ri-CoDIFy 1 and Ri-CoDIFy 2 Phase III clinical trials for ridinilazole. In February 2020, we achieved the first of these patient enrollment targets to trigger a milestone payment of $1.0 million. In September 2021, we reached the second enrollment milestone and earned $1.25 million. In addition, we could receive an additional $1.5 million in various development milestones. We are eligible to receive a further $1.0 million in development milestones, $2.4 million in commercial milestones and up to $18.0 million in sales milestones when cumulative net sales equal or exceed $100.0 million in the Eurofarma licensed territory. Each subsequent achievement of an additional $100.0 million in cumulative net sales will result in Summit receiving additional milestone payments, which, when combined with anticipated product supply transfer payments from Eurofarma paid to us in connection with a commercial supply agreement to be entered into between the two parties, will provide payments estimated to range from a mid-teens to high-teens percentage of cumulative net sales in the Eurofarma licensed territory. We estimate such product supply transfer payments from Eurofarma will range from a high single-digit to low double-digit percentage of cumulative net sales in the licensed territory.

Regulatory and Commercial

Under the license agreement, Eurofarma is responsible for all costs related to obtaining regulatory approval of ridinilazole in the licensed territory and is obligated to use commercially reasonable efforts to file applications for regulatory approval in specified countries in the licensed territory within a specified time period after we have filed an application for regulatory approval, or obtained regulatory approval, for ridinilazole in a jurisdiction where we retain commercial rights. We retain sole responsibility for the clinical development of ridinilazole in all countries and are responsible for all costs related to obtaining regulatory approval for ridinilazole outside of the licensed territory.

We are obligated to use commercially reasonable efforts to supply or cause to be supplied to Eurofarma sufficient commercial supply of ridinilazole, and Eurofarma has agreed to purchase its supply of ridinilazole exclusively from us. If we are unable to supply Eurofarma with commercial supply of ridinilazole during the term of the agreement, we are obligated to transfer to

Eurofarma or its third-party suppliers' know-how that would be needed for Eurofarma or its third-party suppliers to manufacture the product for commercial sale in the licensed territory.

CARB-X

In July 2018, we were granted a sub-award of up to $4.5 million from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program ("CARB-X") to fund, in part, the development of new mechanism antibiotics for the potential treatment of infections caused by gonorrhea. Under our CARB-X award, we received an initial $2.0 million in funding from CARB-X in July 2018. In February 2020, CARB-X increased the value of the initial funding by $1.2 million. The remaining $2.5 million was split into two option segments. In the third quarter of 2020, we made the decision not to advance the DDS-01 series of antibiotics and to cease work on the gonorrhoeae program based on toxicology data from preclinical studies. Given we have ceased work on the DDS-01 series in 2020, no additional funding has been received by CARB-X in 2021 pursuant to this sub-award.

In May 2021, we announced the selection of a new preclinical candidate, SMT-738, which originated from the DDS-04 series. SMT-738 is being developed to combat multi-drug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. Simultaneously, Summit has received a sub-award from CARB-X to progress SMT-738 through preclinical development and an option to continue into Phase Ia clinical studies. The award commits initial non-dilutive funding of up to $4.1 million for the preclinical phase, with the potential for a further $3.7 million available for the Phase Ia clinical phase upon successfully achieving key preclinical development milestones. As of December 31, 2021, $0.5 million of grant funding from CARB-X has been received, $0.1 million is in accounts receivable for amounts billed, $0.6 million is in other current assets as a contract asset and we have recognized $1.2 million of cumulative income since contract inception.

University College London

On March 23, 2010, we entered into a collaborative research agreement with the School of Pharmacy, University of London which was later novated on November 28, 2011, by the School of Pharmacy to University College London. As part of this agreement, and in consideration of their role in the development of the initial compound series from which ridinilazole was later identified, we agreed to pay the School of Pharmacy (now University College London) a low single-digit share of all revenue received by us in respect of ridinilazole, including any pre-commercial licensing revenue, up to a maximum of £1.0 million. To date, we have paid £0.1 million under this agreement.

Discuva Limited Acquisition

Share Purchase Agreement

In December 2017, we entered into a share purchase agreement with the shareholders of Discuva, a private limited company organized under the laws of England and Wales pursuant to which we acquired all of the outstanding share capital of Discuva. Discuva was a discovery-stage company with a bacterial genetics-based platform that facilitates the discovery and development of new mechanism antibiotics.

Under the terms of the share purchase agreement, we paid the Discuva shareholders a total upfront consideration comprised of (A) $6.7 million in cash plus an amount equal to the cash and cash equivalents of Discuva minus (i) indebtedness, (ii) any other liabilities of Discuva at the closing of the transaction that had arisen outside of the ordinary course of business and (iii) funds to be held in escrow and (B) $6.7 million of shares of common stock, satisfied by the issue of 586,685 of our fully-paid shares of common stock at a price per share of $11.41. We made payment of the amount held in escrow, and an additional balancing amount in respect of the closing cash position was made to the Discuva shareholders in December 2018.

In addition, the Discuva shareholders will be entitled to receive contingent payments from us based on (i) the receipt of potential research and development tax credits to which Discuva may be entitled for the period from April 1, 2015, to the date of the share purchase agreement and (ii) approximately one-half of the economic benefit from any amounts received in connection with certain payments made to us under an existing collaboration agreement between Discuva and F. Hoffman - La Roche Limited, or Roche. We made two contingent payments to the Discuva shareholders in December 2018 and May 2019 totaling $1.0 million in respect of research and development tax credits for the period from April 2015 to December 2017 (when the acquisition occurred). Separately, certain employees, former employees and former directors of Discuva are eligible for further payments from Discuva of up to $10.6 million based on specified development and clinical milestones related to proprietary product candidates developed under the platform.

The share purchase agreement contained customary representations and warranties that we and the selling Discuva shareholders made to each other as of specific dates. The assertions embodied in those representations and warranties were made solely for purposes of the share purchase agreement and may be subject to important qualifications and limitations agreed to by us and the Discuva shareholders in connection with negotiating its terms. Moreover, the representations and warranties may be subject to a contractual standard of materiality that may be different from what may be viewed as material to shareholders or may have been

used for the purpose of allocating risk between us and the Discuva shareholders rather than establishing matters as facts. For the foregoing reasons, no person should rely on such representations and warranties as statements of factual information at the time they were made or otherwise.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience, and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies, and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain marketing approvals for their products more rapidly than we obtain approval for ours. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

The key competitive factors affecting the success of our product candidates are likely to be their efficacy, safety, convenience, price and the availability of coverage, and reimbursement from government and other third-party payors.

The competition for ridinilazole includes the following:

Several pharmaceutical and biotechnology companies have established themselves in the market for the treatment of CDI, and several additional companies are developing products for the treatment of CDI. We expect that these products will compete with ridinilazole.

Antibiotics. Currently, the most commonly used treatments for CDI are the broad-spectrum antibiotics vancomycin and metronidazole, both of which are available in generic form in the United States. Generic antibiotic therapies typically are sold at lower prices than branded antibiotics and generally are preferred by managed care providers of health services. The antibiotic fidaxomicin (Dificid™ in the United States, Dificlir™ in Europe) is approved for the treatment of CDI in the United States, Japan and the European Union. Fidaxomicin was originally developed by Optimer Pharmaceuticals, Inc., which was later acquired by Cubist Pharmaceuticals, Inc., or Cubist. Cubist was subsequently acquired by Merck & Co., Inc., or Merck.

MGB Biopharma Limited is developing MGB-BP-3, a novel antibiotic. In May 2020, top-line results were announced that MGB-BP-3 met endpoints of safety, efficacy and dose selection in an open label, exploratory Phase IIa clinical trial. In January 2021, the company announced a successful end-of-phase II meeting with the FDA, noting the FDA confirmed that the design and the endpoints of their two prospective Phase III studies were appropriate.

Acurx Pharmaceuticals Inc. is developing ibezopolstat, a novel antibiotic. In November 2020, top-line results were announced that ibezopolstat met endpoints for efficacy and was reported to be well tolerated with no serious adverse events in an open label, exploratory Phase IIa clinical trial, and ibezopolstat is currently enrolling in a Phase IIb clinical trial.

Other CDI approaches. A number of other approaches for the reduction of recurrence of or prevention of CDI are recently approved or in development. One product, bezlotoxumab, has been approved with the indication of reduction of recurrence of CDI. Merck received FDA approval for the monoclonal antibody bezlotoxumab (Zinplava™) in October 2016 and EMA approval in January 2017. Bezlotoxumab is an antibody that neutralizes certain toxins that are produced by C. difficile bacteria and is indicated to reduce recurrence of CDI in patients who are receiving CDI drug treatment and are at high risk of CDI recurrence. An alternative approach to reduce the rate of CDI recurrence is fecal biotherapy, in which products aim to recolonize the bacteria that comprise the natural gut microbiome. These products would be adjunctive therapy to antibiotics used to treat the episode of CDI. Fecal biotherapy approaches in development include SER-109, which is being developed by Seres Therapeutics Inc., formerly Seres Health, Inc., RBX2660, and enema formulation, and RBX7455, an oral formulation, which were originally being developed by Rebiotix Inc., prior to Rebiotix being acquired by Ferring Pharmaceuticals in April 2018, and CP101, which is being developed by Finch Therapeutics. Seres reported top-line results from a Phase III clinical trial

of SER-109 in August 2020. The trial met its primary endpoint and Seres expects to meet with the FDA to discuss a potential filing for regulatory approval based on the Phase III data. In May 2020, Rebiotix reported positive preliminary results on the primary efficacy measure from one of its two scheduled Phase III clinical trials of RBX2660; its second Phase III trial is currently enrolling patients. Finch Therapeutics announced positive top-line data from its Phase II clinical trial of CP101 related to the reduction of recurrent episodes of CDI.

Several organizations are exploring compounds for the prevention of CDI. Pfizer is developing a vaccine, PF-06425090, that aims to induce a functional antibody response to neutralize the C. difficile bacterial toxins. Pfizer reported positive top-line Phase II results in January 2017. Pfizer entered Phase III testing in 2017, and recently announced results in March 2022. The Phase III trial did not meet its pre-specified primary endpoint of prevention of primary CDI, but two secondary endpoints indicate a highly favorable benefit in reducing CDI severity. Synthetic Biologics, Inc., is developing ribaxamase, an oral enzyme designed to degrade certain IV beta-lactam antibiotics within the GI tract to preserve the natural balance of the microbiome and reduce the risk of colonization by bacteria, including C. difficile, in order to prevent CDI. In January 2017, it was reported that ribaxamase met its primary endpoint in a Phase IIb clinical trial and in November 2018, it announced that it has successfully completed an end-of-Phase II meeting with the FDA to discuss the development of ribaxamase. Pursuant to the meeting, the FDA has proposed criteria for Phase III clinical efficacy and safety which, if achieved, may support submission for marketing approval of ribaxamase on the basis of a single Phase III clinical efficacy and safety, which if achieved, may support submission for marketing approval of ribaxamase on the basis of a single Phase III clinical trial. Da Volterra is developing DAV132, a colon-targeted adsorbent designed to protect the gut microbiome of patients against antibiotic-induced disruption, thus seeking to prevent CDI. DAV132 met its primary endpoint related to safety of DAV132 in a Phase II clinical trial, announced in February 2020. A Phase III trial has commenced with the first patient randomized in July 2021. In November 2020 Destiny Pharma acquired global rights to NTCD-M3, a naturally occurring, non-toxigenic strain of C. difficile bacteria, which lacks the genes that can express C. difficile toxins, for the prevention of recurring CDI. Phase III studies are planned to start in 2022.

Manufacturing

We do not own or operate, and currently have no plans to establish, manufacturing facilities for the production of clinical or commercial quantities of ridinilazole or for the other compounds that we are evaluating in our infectious disease programs. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any products that we may develop.

We currently engage a third-party manufacturer to provide clinical material of the API of ridinilazole with a different supplier responsible for drug product manufacturing services that has supplied the final drug product for use in the Phase III clinical program. We believe these suppliers are suitable for commercial manufacture. We are using a different third-party supplier for clinical packaging, labeling and distribution of the finalized ridinilazole drug product. We obtain the supplies of our API and drug products from these manufacturers pursuant to agreements that include specific supply timelines and volume expectations.

We obtain the supplies of our product candidates from these manufacturers under master services contracts and specific work orders. We do not currently have arrangements in place for redundant supply or a second source for API for ridinilazole. If any of our current manufacturers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might incur some delay in identifying and qualifying such replacements.

All of our product candidates are organic compounds of low molecular weight and are referred to as small molecules. We have selected these compounds based on their potential efficacy and safety, although they are also associated with reasonable cost of goods, ready availability of starting materials and ease of synthesis. We believe that the chemistry for ridinilazole is amenable to scale-up. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Intellectual Property

Our success depends in large part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We strive to protect the proprietary technology that we believe is important to our business by, among other methods, seeking and maintaining patents, where available, that are intended to cover our product candidates, compositions and formulations, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary and competitive position.

As of December 31, 2021, we owned or exclusively licensed a total of 6 U.S. patents, 2 U.S. patent applications, 5 European patents and 4 European patent applications, including original filings, continuations and divisional applications, as well as numerous other foreign counterparts to these U.S. and European patents and patent applications. Our patent portfolio currently contains a total of 80 patents and patent applications.

Discuva Platform Technology. Our Discuva platform technology is currently protected by 12 U.S. and foreign patents, and two pending patent applications. We expect patent protection for this portfolio to expire in 2032.

***Ridinilazole Program*.** Our ridinilazole program is currently protected by 23 granted U.S. and foreign patents, with 3 pending patent applications. The patent portfolio directed to ridinilazole includes patents and patent applications directed to composition of matter, polymorphic forms, methods of manufacture and use, and formulation subject matter. We expect that our existing patents and patent applications (assuming the applications proceed to grant) will provide patent coverage for our ridinilazole program until 2042.

***SMT-738 Program*.** Our SMT738 program currently has 30 patent applications pending worldwide, directed to the composition of matter. We anticipate that our existing portfolio (assuming the applications proceed to grant) will provide patent coverage for our SMT738 program until 2042.

***Patent Term Extension*.** Patent term extensions are available in the U.S. and in some foreign countries, to compensate a patentee for patent term lost between patent grant and obtaining marketing approval by a regulatory agency, such as the FDA, for a product that is protected by the patent. In accordance with the patent term extension provision of the Drug Price Competition and Patent Term Restoration Act, better known as the "Hatch-Waxman Act", an extension of time may be granted for one of Summit's patents protecting ridinilazole, for example, which patent was granted several years before we may obtain marketing approval for the drug product. This extension may provide up to an additional five years of patent term. Similarly, patent extensions called supplementary protection certificates or "SPCs" may be obtained in some foreign countries for patents granted in advance of obtaining market authorization. SPCs may also provide up to an additional five years of patent term. Summit will submit applications for patent term extensions in all countries where such extensions are available to extend patent protection for ridinilazole, as well as for future patents granted that are directed to Summit's other drug programs in development. The expiration dates referred to above are without regard to any potential patent term extension or other extension that may be available in the U.S. or any other market.

***Pediatric Exclusivity*.** Pediatric exclusivity is another type of marketing exclusivity in the U.S. that, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, as well as any patent term that is listed in the FDA "Orange Book" for the corresponding drug product. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather if the pediatric clinical trial is deemed to fairly respond to the FDA's request, and reports of the requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, the additional six months exclusivity is granted. A six-month pediatric extension of a SPC may also be obtained in some foreign countries, subject to carrying out an agreed pediatric investigation plan and compliance with other regulatory requirements of that country.

***Trade Secrets*.** In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third-party. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems.

***Trademarks*.** Summit is in the process of selecting a name for our ridinilazole product, which we will pursue protection for as a trademark in the U.S. and foreign jurisdictions around the world. In connection with the development of our product pipeline, we will seek protection for marks we currently use and future marks when appropriate.

We may not be able to obtain, maintain or protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of third parties. For more information, please see the section on "Risk Factors – Risks Related to Intellectual Property."

Clinical Affairs

We have robust engagements with nationally and internationally recognized key opinions leaders ("KOLs") in research and clinical management of CDI. These KOLs are important in professional societies, peer education, and research and evidence generation, and are assisting us with educational initiatives and clinical development plans. We have a strong publication track record and anticipate multiple presentations at scientific conferences this year to establish ourselves as leaders in *C. difficile* and the gut microbiome.

Sales, Marketing and Market Access

At the present time, we in the process of evaluating the future path forward for our Phase III product candidate, including potential partnership opportunities. In light of this, we believe that our current capabilities with respect to building out a commercial team are adequate for ridinilazole and SMT-738.

Government Regulation

As a biopharmaceutical company focused on the discovery, development, and commercialization of novel antibiotics for serious infectious diseases, we are subject to extensive and ongoing regulation by the FDA under the Federal Food, Drug, and Cosmetic Act and its implementing regulations, as well as other regulatory bodies in the United States and Europe. Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, record keeping, labeling, pricing, reimbursement, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with the FDCA and applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other federal and state governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with current good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, where applicable, and any post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the active pharmaceutical ingredient, or API, and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Companies usually must complete some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the candidate product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested. Stability studies must be conducted to demonstrate that the candidate product does not undergo unacceptable deterioration over its shelf-life.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent
protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls, or CMC. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold.

Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase II or Phase III study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy. Running clinical trials that can support regulatory approvals is the best way to ultimately ensure wide access for patients to our product candidates. At this point in the development, we cannot support any use of our product candidates outside of our clinical trials.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase I. The investigational drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase II. The investigational drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase III. The investigational drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. These clinical trials are commonly referred to as “pivotal” studies, which denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine the primary basis of whether or not to approve a product candidate.

Progress reports of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase I, Phase II and Phase III clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the

product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Under the Pediatric Research Equity Act ("PREA") of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, FDA is to provide sponsors with its best judgment on whether pediatric studies would be required and whether their submission would be deferred until after approval. This input is to be given by the FDA at the end-of-phase I meeting, for drugs for life-threatening diseases, and at the end-of-phase II meeting, for other drugs. A sponsor must submit an initial pediatric study plan, if required under PREA, no later than either 60 calendar days after the date of the end-of-phase II meeting or such other time as agreed upon between FDA and the sponsor.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2022 is $3,117,218 for an application requiring clinical data. The sponsor of the approved NDA is also subject to an annual program fee, which for the fiscal year 2022 is $369,413. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an application, the FDA conducts a filing review of an NDA within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA has agreed to certain performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of new molecular entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to

inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast-track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for fast-track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast-track products, sponsors may have greater interactions with the FDA, and the FDA may initiate review of sections of a fast-track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast-track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast-track application does not begin until the last section of the application is submitted. In addition, the fast-track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, with passage of the 21st Century Cures Act, or Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of antibacterial products *via* the limited-population antibacterial drug (LPAD) pathway. The LPAD pathway provides a unique mechanism for the Food and Drug Administration to review and approve new antibacterial drugs that address unmet medical needs for specific, limited populations of patients - those with serious and life-threatening bacterial infections that are resistant to current treatments. This targeted approach would make antibiotic development more feasible by allowing for smaller clinical development programs that are focused on the limited, high-risk populations that would use these new antibiotics, instead of on more general populations that can be treated with existing medicines. LPAD would also make antibiotic development more feasible by enabling FDA to assess these drugs based on the unique balance of benefits they offer vs. risks they present to the limited number of patients they are intended to treat - specifically, patients who have few or no other treatment options. Product candidates that qualify for LPAD review may simultaneously qualify for one or more of FDA's expedited review programs.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a drug when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase IV or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Limited Population Antibacterial Drug Pathway

With passage of the Cures Act, Congress authorized the FDA to approve an antibacterial or antifungal drug, alone or in combination with one or more other drugs, as a "limited population drug." To qualify for this approval pathway, the drug must be intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs; the standards for approval of drugs and biologics under the FDCA and the Public Health Service Act, or PHSA, must be satisfied; and the FDA must receive a written request from the sponsor to approve the drug as a limited population drug pursuant to this provision. The FDA's determination of safety and effectiveness for such a product must reflect the benefit-risk profile of such drug in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative treatment in such a limited population.

Any drug or biologic approved under this pathway must be labeled with the statement "Limited Population" in a prominent manner and adjacent to the proprietary name of the drug or biological product. The prescribing information must also state that the drug is indicated for use in a limited and specific population of patients and copies of all promotional materials relating to the drug must be submitted to the FDA at least 30 days prior to dissemination of the materials. If the FDA subsequently approves the drug for a broader indication, the agency may remove any post-marketing conditions, including requirements with respect to labeling and review of promotional materials applicable to the product. Nothing in this pathway to approval of a limited population drug prevents sponsors of such products from seeking designation or approval under other provisions of the FDCA, such as accelerated approval.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase IV clinical

trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record keeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fee requirements for any marketed products, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies. The drug manufacturers are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third- party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. Regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCSA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription

pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

GAIN Exclusivity for Antibiotics

In July 2015, the FDA has designated ridinilazole as a qualified infectious disease product, or "QIDP", under the Generating Antibiotic Incentives Now Act, or GAIN Act. In 2019, the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services, or CDC, published an update of its 2013 report reviewing antibiotic resistance threats to the United States. This updated report continued to highlight that CDI poses an immediate public health threat that requires urgent and aggressive action, and *C. difficile* is one of four bacterial pathogens with this urgent threat status. Congress passed this legislation to encourage the development of antibacterial and antifungal drug products that treat pathogens that cause serious and life-threatening infections. To that end, the GAIN Act grants an additional five years of exclusivity upon the approval of an NDA for a drug product designated by the FDA as a QIDP. Thus, for a QIDP, the periods of five-year new chemical entity exclusivity, three-year new clinical investigation exclusivity and seven-year orphan drug exclusivity, would become ten years, eight years and 12 years, respectively.

A QIDP is defined in the GAIN Act to mean "an antibacterial or antifungal drug for human use intended to treat serious or life- threatening infections, including those caused by: (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens;" or (2) certain "qualifying pathogens." A "qualifying pathogen" is a pathogen that has the potential to pose a serious threat to public health (such as resistant Gram-positive pathogens, multi-drug resistant Gram- negative bacteria, multi-drug resistant tuberculosis and *Clostridioides difficile*) and that is included in a list established and maintained by the FDA. A drug sponsor may request the FDA to designate its product as a QIDP any time before the submission of an NDA. The FDA must make a QIDP determination within 60 days of the designation request. A product designated as a QIDP will be granted priority review by FDA and can qualify for "fast track" status.
The additional five years of exclusivity under the GAIN Act for drug products designated by the FDA as QIDPs applies only to a drug that is first approved on or after July 9, 2012. Additionally, the five year exclusivity extension does not apply to: a supplement to an application under FDCA Section 505(b) for any QIDP for which an extension is in effect or has expired; a subsequent application filed with respect to a product approved by the FDA for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or a product that does not meet the definition of a QIDP under Section 505(g) based upon its approved uses.

Patent Term Restoration and Extension

The term of a U.S. patent that covers a drug, biological product or medical device approved pursuant to a PMA may also be eligible for patent term extension when FDA approval is granted, provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug may be extended. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug, provided that statutory and regulatory requirements are met. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure

regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Regulation and Marketing Authorization in the European Union

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual E.U. Member States govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the
E.U. Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual E.U. Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (E.U.) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation was published on June 16, 2014, but has not yet become effective. The Clinical Trials Regulation will be directly applicable in all the E.U. Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure *via* a single entry point, the "E.U. Portal and Database;" a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all E.U. Member States in which an application for authorization of a clinical trial has been submitted (Concerned Member States). Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

As of January 1, 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation ("CTR") was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. The European Commission published a notice in the Official Journal of the European Union on July 31, 2021 confirming January 31, 2022 as the date of entry into application of the Clinical Trials Regulation and the go-live of its Clinical Trials Information System ("CTIS").

As in the United States, similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries.

Marketing Authorization

To obtain a marketing authorization for a product under E.U. regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the E.U. Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the E.U. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e., the European Union as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, ATMPs and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the

request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of E.U. law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the E.U. Member States and chaired by a non- voting European Commission representative. The European Parliament also has a related "droit de regard." The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances." Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The E.U. medicines rules expressly permit the E.U. Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain E.U. Member States may prohibit or restrict us from commercializing our products, even if they have been granted an E.U. marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each E.U. Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the

centralized procedure. The referenced E.U. Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned E.U. Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned E.U. Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all E.U. Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the E.U. Member States of the marketing authorization of a medicinal product by the competent authorities of other E.U. Member States. The holder of a national marketing authorization may submit an application to the competent authority of an E.U. Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another E.U. Member State.

Regulatory Data Protection in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance to the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the E.U. market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the E.U. Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the E.U. Member States decide on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the E.U. market (in case of centralized procedure) or on the market of the authorizing E.U. Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Pediatric Studies

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable E.U. laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with E.U. cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83EC, as amended, and E.U. Member State laws. Direct-to- consumer advertising of prescription medicines is prohibited across the European Union.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom withdrew from the European Union on January 31, 2020. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, European Union rules have ceased to apply following the transition period which ended December 31, 2020. However, in December 2020, the United Kingdom and the European Union agreed on a trade and cooperation agreement that will apply provisionally after the end of the transition period until it is ratified by the parties to the agreement. The United Kingdom has passed legislation giving effect to the trade and cooperation agreement, with the E.U. expected to formally adopt the agreement in early 2021. The trade and cooperation agreement provides a general framework for the post-withdrawal relationship between the United Kingdom and the European Union. We expect to be subject to additional and potentially duplicative regulatory requirements due to the withdrawal of the United Kingdom from the European Union, including requirements relevant to receiving marketing approval for ridinilazole. However there remains substantial uncertainty related to the implementation of the trade and cooperation agreement and the application of its terms.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the E.U. General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pricing Decisions for Approved Products

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so- called health technology assessments in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high- priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Patent Term Extension

In order to compensate the patentee for delays in obtaining a marketing authorization for a patented product, a supplementary certificate, or SPC, may be granted extending the exclusivity period for that specific product by up to five years. Applications for SPCs must be made to the relevant patent office in each E.U. member state and the granted certificates are valid only in the member state of grant. An application has to be made by the patent owner within six months of the first marketing authorization being granted in the European Union (assuming the patent in question has not expired, lapsed or been revoked) or within six months of the grant of the patent (if the marketing authorization is granted first). In the context of SPCs, the term "product" means the active ingredient or combination of active ingredients for a medicinal product and the term "patent" means a patent protecting such a product or a new manufacturing process or application for it. The duration of an SPC is calculated as the difference between the patent's filing date and the date of the first marketing authorization, minus five years, subject to a maximum term of five years.

A six month pediatric extension of an SPC may be obtained where the patentee has carried out an agreed pediatric investigation plan, the authorized product information includes information on the results of the studies and the product is authorized in all member states of the European Union.

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-government third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products.

Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. In March 2010, the United States Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 70% as of January 1, 2019 point-of-sale-discount off the negotiated price of applicable brand drugs to eligible

beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in additional pricing pressures. The demand for our products is predicated on our clinical trial strategy of attempting to achieve superiority against the standard-of-care. If there are not adequate reimbursement levels, our business and results of operations could be adversely affected.

Human Capital

In order to be a competitive, innovative and successful Company, we believe it is critical to attract, engage, motivate and retain a dedicated, talented and innovative team of employees. As part of these efforts, we strive to foster a diverse, equitable and inclusive community, invest in continuous learning and development, offer a competitive compensation and benefits program and provide a safe and healthy workplace. Our success starts and ends with having the best talent and, as a result, we are focused on attracting, developing, and engaging our employees. In 2021, Summit has notably strengthened the team by continuing to attract a number of leading world class employees into the Company. These new recruits have successful track records and are acknowledged leaders in their field.

As of December 31, 2021, we had 105 full-time employees and 110 total employees. Of our total workforce, approximately 67% work in research and development, and 33% work in finance, legal, information technology, general management and other administrative functions. Approximately 60% and 40% of our workforce is located in the U.S. and the U.K., respectively.

In 2021, we once again made challenging demands of our employees and they have responded with dedication and enthusiasm. In 2021, Summit launched an engagement survey, in which over 80% of employees responded. The results of this survey reflected an overall positive response by employees, particularly highlighting both the enjoyment of their work and the team they work with.

Compensation and Benefits

We provide robust compensation and benefits programs to attract, motivate and retain our employees. In addition to competitive compensation, we provide generous benefits including employer contributions to pension/401k plans, an employee stock purchase plan, insurance benefits, healthcare programs and paid vacation. We are committed to ensuring that our total compensation packages are competitive while supporting our business plans and strategies.

Diversity, Equity and Inclusion

We are committed to embedding a culture of diversity, equity and inclusion across our Company. We believe that diversity of gender, race, ethnicity, sexual orientation, culture, education, background and experience fuels innovation and enables our employees to succeed. This includes ensuring opportunity for all and embraces the positive effect that our diverse workforce brings. We do not tolerate any form of discrimination and our employment policies and practices focus on ensuring that all our employment processes are free from discrimination or harassment on any grounds. Approximately 60% of our employees are female and 62% of our executive team is female.

Learning and Development

We are committed to investing in learning and development for our employees. Our employees have access to online training courses which cover a wide range of technical and business topics to help them develop their professional skills and explore other areas as they plan for their career and personal growth. Our performance management process includes timely performance feedback and career development discussions which are critical to each employee's continued growth and development within the organization.

Workplace Health and Safety and Pandemic Response

We are committed to the health and safety of all of our employees. We accomplish this through strict compliance with applicable laws and regulations regarding workplace safety. We have continued to maintain our focus on the health and safety of our employees especially as the COVID-19 pandemic has evolved, including maintaining protocols for social distancing, daily onsite health checks and allowing our employees to work remotely as necessary based upon local government health recommendations. Our experienced teams continue to adapt quickly to the changes and have managed our business successfully during this challenging time.

Our Corporate Information

On September 18, 2020, pursuant to a scheme of arrangement under UK law, we became the parent company of the Summit Therapeutics plc group of companies, including Summit Therapeutics plc, a public limited company incorporated under the laws of England and Wales with the Registrar of Companies of England and Wales. Pursuant to the scheme of arrangement, all outstanding ordinary shares of Summit Therapeutics plc were exchanged for shares of our common stock on a five for one basis.

In connection with the scheme of arrangement, Summit changed its corporate domicile from the United Kingdom to Delaware. Our principal executive offices are located at One Broadway, 14th Floor, Cambridge, MA States 02142, and our telephone number is +1 617 514 7149. Our website address is www.summittxinc.com. The information contained on, or that can be accessed through, our website is not incorporated by reference into this Report or in any other report or document we file with the SEC, and any reference to our website address is intended to be an inactive textual reference only.

We own or have rights to trademarks, service marks, and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks, and trade names appearing in this Report are the property of their respective owners. Solely for convenience, some of the trademarks, service marks, and trade names referred to in this Report are listed without the ® and ™ symbols.

Available Information

We are the successor to Summit Therapeutics plc for various purposes under the Exchange Act and, through the filing of a Current Report on Form 8-K filed pursuant to Rule 12g-3 under the Exchange Act, have assumed Summit Therapeutics plc's Commission file number (001-36866). We began filing reports under the Exchange Act with the filing of that Current Report on Form 8-K. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act will be posted on our website as soon as reasonably practicable after electronic filing with or furnishing to the Securities and Exchange Commission and the Annual Reports on Form 20-F and Reports on Form 6-K filed by Summit Therapeutics plc prior to the completion of the Redomiciliation Transaction are available on our website. All such postings on our website can be accessed free of charge.

Item 1A. Risk Factors

This section describes certain risks we face in our business. Additional risks we do not yet know of or that we currently believe are immaterial may also impair our business. If any of the events or circumstances described in this section actually occurs, our business, financial condition or operating results could suffer, and the market price of our common stock could decline. In assessing these risks, investors should also refer to the other information contained or incorporated by reference in this report and our other filings with the Securities and Exchange Commission.

Risks Related to our Financial Position and Need for Additional Capital

We depend heavily on the success of our product candidates. We may not be able to identify third-party partnership opportunities with whom to commercialize our product candidates. If we are unable to successfully commercialize our product candidates through a partnership, or experience significant delays in doing so, we may extend the period in which we will incur significant financial losses as an organization.

We plan to seek one or more third party partnership arrangements for potential additional clinical development and commercialization of our lead product candidate, ridinilazole, which we are developing for the treatment of CDI. Our ability to generate revenues from these arrangements will depend on our partners' abilities and efforts to successfully perform the functions assigned to them in these arrangements. If we are unable to establish a partnership, or if such a partnership is not successful, we may not be able to capitalize on the market potential of these product candidates.

Third party partnerships involving our product candidates pose a number of risks, including the following:

- third-party partners have significant discretion in determining the amount and timing of efforts and resources that they will apply to these third-party partnerships;
- third-party partners may not perform their obligations as expected;
- third-party partners may not pursue commercialization and development of our product candidates that receive marketing approval or may elect not to continue or renew commercialization or development programs based on clinical trial results, changes in the partners' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- third-party partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- third-party partners could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the partners believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered under third-party partnerships with us may be viewed by our third-party partners as competitive with their own product candidates or products, which may cause partners or licensees to cease to devote resources to the commercialization of our product candidates;
- a third-party partner with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with third-party partners, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and expensive;
- third-party partners may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- third-party partners may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- third-party partners may be terminated for the convenience of the third-party partner and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Third-party partnership agreements may not lead to commercialization or development of product candidates in the most efficient manner, or at all. If any partnerships that we enter into, do not result in the successful commercialization and development of products or if one of our partners terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the commercialization partnership. Additionally, if one of our partners

terminates its agreement with us, we may find it more difficult to attract new partners and our perception in the business and financial communities could be harmed.

We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never generate profits from operations or maintain profitability.

We are a development-stage company and we cannot assure profitability. We expect to continue to generate operating losses for the foreseeable future. Until we can generate substantial revenue and achieve profitability, we will need to raise additional capital to fund ongoing operations and capital needs. Since inception, we have incurred significant operating losses. During year ended December 31, 2021, we incurred a net loss of $88.6 million, and cash flows used in operating activities was $72.6 million. As of December 31, 2021, we had an accumulated deficit of $299.5 million, cash of $71.8 million, research and development tax credits of $15.7 million and accounts receivable of $1.5 million. Based on our current funding arrangements and financial resources as of December 31, 2021 and after considering proceeds received of $25.0 million from the 2022 Note issued on March 10, 2022, the Company has the ability to funds its operating costs and working capital needs into the second half of 2023. We expect to continue to generate operating losses for the foreseeable future. Until we can generate substantial revenue and achieve profitability, we will need to raise additional capital to fund ongoing operations and capital needs.

To date, we have financed our operations primarily through issuances of our common stock (and before the Redomiciliation Transaction issuances of Summit Therapeutics plc's ordinary shares and American Depositary Shares), payments to us under our license and commercialization agreement with Eurofarma, and development funding and other assistance from government entities, philanthropic, non-government and not for profit organizations. In particular, we have received funding from BARDA, CARB-X, Innovate UK, Wellcome Trust and a number of not-for-profit organizations.

We have devoted substantially all of our financial resources and efforts to developing our lead product candidate, ridinilazole, for the treatment of CDI, identifying potential product candidates, and conducting preclinical studies and clinical trials. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses may increase substantially as we:

- conclude and assess our Ri-CoDIFy Phase III trial's data for our lead product candidate, ridinilazole, for the treatment of CDI and consider the future path forward, including potential partnership opportunities;
- conduct research and continue preclinical development of additional product candidates;
- maintain and augment our intellectual property portfolio and opportunistically acquire complimentary intellectual property;
- seek further regulatory advancement for ridinilazole;
- invest in our manufacturing capabilities for ridinilazole and any other products for which we may obtain regulatory approval;
- perform our obligations under our collaboration agreements;
- pursue business development opportunities, including investing in other businesses, products and technologies;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges

To become and remain profitable, we must succeed in developing and eventually either commercializing or partnering with other organizations to commercialize products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing, and selling any products for which we may obtain regulatory approval. We are in the preliminary stages of many of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product and biological development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, developing and securing our technology, raising capital and undertaking preclinical studies and clinical trials of our product candidates. We have not yet demonstrated our ability to successfully complete development of any product candidates, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities or otherwise obtain a partner to do so as is necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Assuming we obtain marketing approval for any of our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities or seek an appropriate partner or partners to maximize the commercial opportunity of our products with a deal structure that maximizes our opportunities for profitability. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

We will need substantial additional capital to fund our operations and if we fail to obtain necessary financing, we could be forced to delay, reduce or eliminate the development and commercialization of our product candidates.

We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we seek business development opportunities to clinically develop and ultimately commercialize product candidates. In addition, if we obtain marketing approval these potential future product candidates where we retain commercial rights or any other product candidates we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We do not have any committed external source of funds other than amounts we may receive from Eurofarma, BARDA, CARB-X and under our arrangements with them and our research and development tax credits receivable. As a result, we will need additional capital to fund our operations. Additional capital, when needed, may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we will be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition.

Our future capital requirements will depend on many factors, including:

- the timing and evaluation of the data from our Phase III Ri-CoDIFy clinical trial for our lead product candidate, ridinilazole (formerly SMT19969), the next steps we will take with ridinilazole based upon our review, and the costs associated with these decisions, including completing our review of the data associated with Ri-CoDIFy and any partnerships into which we may enter to continue the advancement of ridinilazole;
- the number and development requirements of other future product candidates that we pursue;
- the costs, timing and outcome of regulatory review of ridinilazole and/or our other product candidates we develop;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- subject to receipt of marketing approval, revenue received from commercial sales of any product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims;
- our ability to establish and maintain collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the extent to which we acquire or invest in other businesses, products and technologies;
- the rate of the expansion of our physical presence;

- the extent to which we change our physical presence

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we are not planning to have commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. Additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our investors, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, collaborations, strategic alliances, grants and clinical trial support from government entities, philanthropic, non-government and not-for-profit organizations and patient advocacy groups, debt financings, and marketing, distribution or licensing arrangements. We do not have any committed external source of funds other than the amounts we are entitled to receive from BARDA under our contract with them to fund, in part, the clinical and regulatory development of ridinilazole and from Eurofarma under our license and commercialization agreement with them. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as an equity holder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to our Financial Dependence on Third Parties

Our reliance on government funding for ridinilazole adds uncertainty to our research and commercialization efforts with respect to ridinilazole.

We expect that a significant portion of the funding for the development of ridinilazole will come from our contract with BARDA until such time we may partner with another party in relation to ridinilazole; although there is no assurance we will be able to enter into such an agreement, or if we do, if all development expenses will be paid by the licensor pursuant to the license agreement. BARDA is entitled to terminate our BARDA contract for convenience at any time, in whole or in part, and there can be no assurance that our BARDA contract will not be terminated. Changes in government budgets and research priorities may result in a decreased and de-prioritized emphasis on supporting the development of antibacterial product candidates such as ridinilazole. If our BARDA contract is terminated or BARDA declines to exercise the final option for the research program, or if there is any reduction or delay in funding under our BARDA contract, we may be forced to seek alternative sources of funding, which may not be available on non-dilutive terms, terms favorable to us, or at all. If alternative sources of funding are not available, we may suspend or terminate development activities related to ridinilazole.

BARDA may elect not to pursue the remaining designated option beyond the base period.

Even if BARDA does not terminate the contract, the BARDA contract does not require BARDA to provide funding beyond the amount currently obligated under the base period and three options packages of the existing contract (with a performance period ending April 2022). The awarded contract was originally worth up to $62.0 million. In June 2019 and again in January 2020, BARDA increased the value of the contract such that it is now worth up to $72.5 million. In August 2018, one of the three option work segments was exercised by BARDA with the $12.0 million in funding to be drawn down to specifically support drug manufacturing activities required for the submission of marketing approval applications and other regulatory activities. In June 2019, a second of the three option work segments was exercised by BARDA with the $9.6 million in funding to be drawn down to support patient enrollment and dosing in the Phase III clinical trials of ridinilazole. Activities to be covered by the remaining option work segment include the preparation, submission and review of applications for marketing approvals of ridinilazole for CDI in the United States. The remaining federal government funding is dependent on BARDA in its sole discretion exercising the final independent option work segment, upon the achievement by the Company of certain agreed-upon milestones for ridinilazole and there can be no assurance that BARDA will elect to pursue the option. If this option work

segment is exercised by BARDA, the contract would run into 2022, unless extended by us and BARDA. Changes in government budgets and research priorities may result in a decreased and de-prioritized emphasis on supporting the development of antibacterial product candidates such as ridinilazole. In such event, BARDA would have no obligation to exercise its remaining option or extend our existing contract. Any such decision by BARDA to end its support for our ridinilazole research program could materially adversely affect our business.

Our reliance on government funding for the clinical and regulatory development of ridinilazole may impose requirements that increase the costs of commercialization and production of product candidates developed with the support of these government-funded programs.

Aspects of our development programs are currently being supported, in part, with funding from BARDA. Contracts and grants awarded by the U.S. government, its agencies and its partners, including our award from BARDA, include provisions that implement the U.S. government's rights and remedies, many of which are not typically found in commercial contracts, including, for example, powers of the government to:

- terminate agreements, in whole or in part, at any time, for any reason or no reason;
- unilaterally modify the parties' obligations under such contracts, subject to government-determined equitable price adjustments;
- decline to exercise any option for work beyond the initial base period under multi-year contracts;
- suspend contract performance if Congressionally appropriated funding becomes unavailable;
- obtain rights to inventions and technical data made or first produced in the performance of such contracts;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend or debar the contractor from receiving new contracts pending resolution of alleged violations of procurement laws or regulations in the event of wrongdoing by us;
- take actions that result in a longer development timeline than expected;
- direct the course of a development program in a manner not chosen by the government contractor;
- impose U.S. manufacturing requirements for products that embody or that are produced through the use of inventions conceived or first reduced to practice under such contracts;
- assert qualified march-in rights to grant licenses to third parties to practice contractor-owned inventions that are conceived or first reduced to practice under such contracts;
- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

We may not have the right to prohibit the U.S. government from using certain inventions and technical data funded by the government and developed by us, and we may not be able to prohibit third-party companies, including our competitors, from using those inventions and technical data in providing products and services to the U.S. government. The U.S. government generally takes the position that it has the right to royalty-free use of inventions and technical data that are developed under U.S. government contracts.

In addition, U.S. government contracts normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These requirements include, for example:

- specialized accounting systems unique to government contracts;
- potential liability for price adjustments or recoupment of government funds after such funds have been spent;
- mandatory disclosure of credible evidence of certain contractual or statutory violations occurring in connection with the contract;
- public disclosures of certain contract information, which may enable competitors to gain insights into our research program; and
- mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

As an organization, we are relatively new to government contracting and the associated regulatory compliance obligations. If we fail to maintain compliance with those obligations, we may be subject to potential civil and/or criminal liability, termination of our BARDA contract, and/or suspension, debarment, or exclusion from eligibility for other U.S. government contracts,

funding programs and regulatory approvals. As a U.S. government contractor, we are subject to financial audits and other reviews by the U.S. government of our costs and performance under our BARDA contract, as well as our accounting and general business practices related to our BARDA contract. Based on the results of its audits, the U.S. government may adjust our contract-related costs and fees, including allocated indirect costs.

We depend on collaborations with third parties for the development and commercialization of some of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have entered into a license and commercialization agreement with Eurofarma pursuant to which we granted Eurofarma rights to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean. We may also enter into additional third-party collaborations for the development and commercialization of ridinilazole in other jurisdictions. Moreover, we may seek third-party collaborators for development and commercialization of any other product candidates.

Our likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Under our license and commercialization agreement with Eurofarma we have, and under any such arrangements we enter into with any third parties in the future we will likely have, limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Our current collaborations pose, and any future collaboration likely will pose, numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a sale or disposition of a business unit or development function, or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;
- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of our product candidates. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of the active pharmaceutical ingredients, or API, in our product candidates. Our strategy is to outsource all manufacturing of our product candidates and products to third parties.

We have agreements with third-party manufacturers for the long-term clinical or commercial supply of our product candidates. We are engaged with a third-party manufacturer to provide clinical material of the API of ridinilazole with a different supplier responsible for fill and finish services to supply the final drug product for use in the Phase III clinical trials. The third-party manufacturers may not successfully carry out their contractual duties or obligations, the occurrence of which could substantially increase our costs and limit our supply of such product candidates. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practice, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

In addition, in order to conduct late-stage clinical trials of our product candidates, we will need to have them manufactured in large quantities. Our third-party manufacturers may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all.

Moreover, if our third-party manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

If the third parties that we engage to manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, including due to the novel coronavirus or another outbreak, we likely would experience delays in advancing these clinical trials while we identify and qualify replacement suppliers, and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively. Any inability to obtain adequate supplies of ridinilazole for clinical trials may also impact Eurofarma's ability to commercialize ridinilazole, if marketing approval is obtained, in the jurisdictions where Eurofarma holds commercialization rights. Under our license and commercialization agreement with Eurofarma, we have agreed to use commercially reasonable efforts to supply or cause to be supplied to Eurofarma sufficient commercial supply of ridinilazole.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability, and the ability of Eurofarma and any other future collaborator, to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis.

We rely on third parties to conduct our clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such clinical trials.

We do not independently conduct clinical trials for our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practice, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity of data and confidentiality of clinical trial participants are protected. The EMA imposes similar requirements on us for products that are the subject of clinical trials in the European Union, including the United Kingdom.

We also are required to register ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, www.ClinicalTrials.gov, within certain timeframes. Failure to comply would violate federal requirements and could result in fines and/or civil and criminal sanctions, which would delay the regulatory approval process and result in adverse publicity.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing approvals.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate further with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators and changes to the strategies of the combined company.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

If we fail to comply with our obligations in our funding arrangements with third parties, we could be required to repay the grant funding we have received or grant to these third parties rights under certain of our intellectual property.

We have received grant funding for some of our development programs from philanthropic, non-government and not-for-profit organizations and patient advocacy groups pursuant to agreements that impose development and commercialization diligence obligations on us. If we fail to comply with these obligations, in certain instances the applicable organization could require us to repay the grant funding we have received with interest or grant to the organization rights under certain of our intellectual property, which could materially adversely affect the value to us of product candidates covered by that intellectual property even if we are entitled to a share of any consideration received by such organization in connection with any subsequent development or commercialization of the product candidates.

Risks Related to Our Industry and Market

We face substantial competition, which may result in others discovering, developing or commercializing products before us or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize whether ourselves or through third-party partners, in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Several pharmaceutical and biotechnology companies have established themselves in the market for the treatment of CDI, and several additional companies are developing products for the treatment of CDI. Currently, the most commonly used treatments for CDI are the broad-spectrum antibiotics vancomycin and metronidazole, both of which are available in generic form in the United States. Generic antibiotic therapies typically are sold at lower prices than branded antibiotics and generally are preferred by managed care providers of health services. The antibiotic fidaxomicin (Dificid™ in the United States and Dificlir™ in Europe), which is marketed in the United States by Cubist Pharmaceuticals, Inc., or Cubist, a wholly owned subsidiary of Merck & Co., Inc., or Merck, and in Europe by Tillotts Pharma AG, is approved for treatment of CDI in the United States and the European Union. Merck received approval from the FDA and EMA for bezlotoxumab (Zinplava™), a monoclonal antibody for the treatment of patients, in combination with an antibiotic, who have a high risk of disease recurrence. Other approaches in development for the treatment of CDI include vaccines and fecal biotherapy. For more information, see “Business—Competition” in this Report.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are approved for broader indications or patient populations, or are more convenient or less expensive than any products that we develop and commercialize. Our competitors may also obtain marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

We believe that many competitors are attempting to develop therapeutics for the target indications of our product candidates, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approvals from regulatory authorities and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs.

We may complete a future acquisition that may not achieve intended results or could increase the number of our outstanding shares or amount of outstanding debt or result in a change of control.

We are pursuing business development opportunities to expand our pipeline of product candidates, including without limitation, through potential acquisitions of and/or collaborations with other entities. Any such transaction could happen at any time, could be material to our business and could take any number of forms, including, for example, an acquisition, merger or a collaboration with other entities.

Any acquisition we consummate will involve the integration of the operations, product candidates and technology of the acquired business with our existing operations and programs, and there are uncertainties inherent in any such integration. Evaluating potential transactions and integrating completed ones are likely to require significant resources and may divert the attention of our management from ordinary operating matters, including the resources and attention required to further the development of any acquired product candidates or other development programs, or the commercialization of any acquired product. The success of these potential transactions will depend, in part, on our ability to realize the anticipated growth opportunities and cost synergies through the successful integration of the businesses we acquire with our existing business, as well as the success of the underlying business or intellectual property that we acquire or otherwise obtain rights to. Unexpected difficulties in the integration process for an acquisition or the failure to retain key management personnel from an acquired business could adversely affect our business, financial results and financial condition. In addition, in any acquisition, the due diligence process may not identify all factors that could produce unintended or unexpected consequences for us. Undiscovered factors could cause us to incur potentially material financial liabilities and prevent us from achieving the expected benefits from the acquisition within our desired timeframe, or at all.

Even if we are successful in integrating the acquired businesses, we cannot assure you that these integrations will result in the realization of the full benefit of any anticipated growth opportunities, intellectual property, or cost synergies or that these benefits will be realized within the expected time frames. In addition, acquired businesses may have unanticipated liabilities or contingencies, or the strategic reasons for the acquisition may not be correct, and the acquisition could not provide the benefits anticipated by management. If we complete an acquisition, investment or other strategic transaction, we will likely require additional financing that could result in a substantial increase in the number of our outstanding shares or the aggregate amount of our debt.

Risks Related to the COVID-19 Pandemic

The ongoing COVID-19 pandemic continues to evolve and its enduring impact on our business remains uncertain. Our business has and could continue to be adversely affected, directly or indirectly, by the ongoing COVID-19 pandemic.

The continual spread of COVID-19 and the emergence of new variants has caused a broad impact globally, adversely affecting the economies and financial markets of many countries and resulting in an economic downturn. These adverse economic effects, as well as the uncertainty regarding the duration, spread and intensity of the pandemic have led to labor shortages, supply restrictions and inflationary pressures. As a result of the COVID-19 pandemic, governmental authorities across the world have implemented and may continue to implement safety precautions. These measures may disrupt normal business operations and may continue to have significant negative impacts on businesses and financial markets worldwide. We continue to monitor our operations and applicable government recommendations, and we have made modifications to our normal operations because of the COVID-19 pandemic, including limiting travel and working from home. Changes in flexible working arrangements could impact employee retention, employees' productivity and morale, strain our technology resources and introduce operational risks. Additionally, the risk of cyber-attacks or other privacy or data security incidents may be heightened as a result of our moving increasingly towards a remote working environment, which may be less secure and more susceptible to hacking attacks. The COVID-19 pandemic could affect the health and availability of our workforce as well as those of the third-parties we rely on. Furthermore, delays and disruptions due to the COVID-19 pandemic experienced by our collaborators or other third-parties, including regulatory agencies, such as the FDA, could adversely impact the ability of such parties to fulfill their obligations.

The disruptions caused by COVID-19, including the limitations on in-person meetings with existing or potential stakeholders may result in inefficiencies, delays and additional costs in our product development, sales, marketing, product implementation and customer service efforts that we may not be able to fully mitigate through remote work arrangements. We have experienced, and expect to continue to experience, patient enrollment at a slower pace at certain of our clinical trial sites than expected. In addition, certain of our clinical trial sites have suspended enrollment due to facility closures, quarantine, travel restrictions and other governmental restrictions. Further, we are currently unable to undertake certain activities directly including clinical trial site visits and investigator meetings, with such activities being done remotely where possible. Our ability to continue our existing clinical trials or to initiate new clinical trials has been and may continue to be adversely affected, directly or indirectly, by the COVID-19 pandemic. While we do not currently anticipate significant interruptions in our clinical supply chain, quarantines, travel restrictions and other measures may significantly impact the ability of employees of our third-party suppliers to get to their places of work to manufacture and deliver additional clinical supplies, which could cause the results from our clinical trials to be delayed even further.

Several vaccines for COVID-19 have been developed and widely distributed in the United States. However, it is unknown how effective they will be long-term or whether variants of the virus will develop against which the vaccines are less effective.
While it is not possible at this time to estimate the entirety of the continued impact the COVID-19 pandemic will have on our business, operations, employees, customers, suppliers or collaboration partners, continued spread of COVID-19, measures

taken by governments, actions taken to protect employees and the broad impact of the pandemic on all business activities may materially and adversely affect our business, supply chain, results of operations and financial condition.

Risks Related to the Development and Commercialization of our Product Candidates

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the U.S. Food and Drug Administration, or the FDA, or the European Medicines Agency, or the EMA, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of ridinilazole or any other product candidate.

In connection with obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In particular, due to the small number of patients in our early clinical trials, results from such trials may not be predictive of the outcome of later clinical trials. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole which showed that ridinilazole resulted in a numerically higher SCR rate than vancomycin, but did not meet the study's primary endpoint for superiority. We are continuing to evaluate the underlying data and perform additional analyses. There is no assurance as to what will be the outcome of our evaluation and analyses, or whether the regulatory authorities, including the FDA, will agree with our determination and conclusion.

In light of the top-line results of the Ri-CoDIFy study, and our decision to move forward with becoming a leader in the microbiome therapeutics space, we have determined that we may seek one or more third party partnership opportunities for ridinilazole. We plan to continue to review our data, including performing additional analyses on the microbiome and the relative impacts of ridinilazole and vancomycin with respect to any additional considerations in terms of advancing ridinilazole. In addition, we may pursue business development opportunities to expand our pipeline of product candidates, including without limitation, through potential acquisitions of and/or collaborations with other entities.

If we experience any number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval for or commercialize our product candidates, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate for various reasons, including due to contagious diseases or illnesses, such as the novel coronavirus, as described below;
- we may be unable to enroll a sufficient number of patients in our clinical trials to ensure adequate statistical power to detect any statistically significant treatment effects;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, institutional review boards or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators, institutional review boards or independent ethics committees may require that we or our investigators materially modify the terms of our clinical research in order to meet additional requirements for receiving marketing approval, including by requiring that we enlarge our trials, broaden the scope of our research, or perform studies in

addition to those we currently anticipate, which may delay our ability to obtain marketing approval or impose additional costs;
- regulators, institutional review boards or independent ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates, comparator drugs or other materials necessary to conduct clinical trials of our product candidates in adolescent patients may be insufficient or inadequate, which may occur if, for example, enrollment for our clinical trial programs are delayed and the clinical supply of ridinilazole or vancomycin manufactured for such trials was not utilized prior to its expiration and needed to be replaced, or if there were disruptions in our supply chain due to weather conditions, natural disasters or contagious diseases or illnesses, such as the novel coronavirus; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the clinical trials.

Our product development costs will increase as we experience delays in testing or marketing approvals. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the
exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in our clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates, if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials. CDI is an acute infection that requires rapid diagnosis. For our Phase III clinical trials of ridinilazole, we need to identify potential patients, test them for CDI and enroll them within three days and prior to patients receiving other antibiotic treatments that may be active against CDI for greater than a 24-hour period. In addition, our competitors in CDI have ongoing clinical trials for product candidates that could be competitive with our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates or choose not to enroll in any clinical trials for various reasons, including due to fears of contagious diseases or illnesses, such as the novel coronavirus.

Patient enrollment is affected by other factors, including:

- severity of the disease under investigation;
- eligibility criteria for the clinical trial in question;
- perceived risks and benefits of the product candidate under study;
- competition for patients, time and resources at clinical trials sites from other investigational therapies in clinical trials that target the same patient population;
- approval of other therapies to treat the indication that is being investigated in the clinical trial;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients in our ongoing clinical trials of ridinilazole or any other planned clinical trials would result in significant delays, may generate a limited data set from which no meaningful conclusions could be made, or may require us to abandon one or more clinical trials altogether.

If serious adverse or inappropriate side effects are identified during the development of ridinilazole or any other product candidate, we may need to abandon or limit our development of that product candidate.

All of our product candidates are in clinical or early-stage development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Although ridinilazole has generally been well tolerated at all doses tested, patients who typically are diagnosed with CDI have a number of underlying illnesses, which means it is more likely that we will see adverse events and serious adverse events being reported even if these events are later deemed to be unrelated to treatment with ridinilazole. For example, in our Phase II proof of concept clinical trial of ridinilazole, a total of 180 adverse events were reported for ridinilazole, although the majority of these were considered unlikely to be related to treatment with ridinilazole, and the number of ridinilazole reported adverse events was similar to patients treated with vancomycin, the comparator drug used in this clinical trial, where a total of 183 adverse events were reported. Most of the adverse events occurred in the gastrointestinal system organ class with nausea, abdominal pain, abdominal distention and vomiting the most commonly reported events for both treatment groups. Often, it is not possible to determine conclusively whether or not the product candidate being studied caused a particular adverse event. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test ridinilazole in a larger clinical program, illnesses, discomforts and other adverse events that were observed in earlier clinical trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by clinical trial patients.

Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects or other safety issues that prevented further development of the compound. If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed and our ability to generate product revenues from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

Even if ridinilazole or any other product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If ridinilazole or any of our other product candidates receive marketing approval, such products may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, it could make it more difficult to enter into third-party partnership arrangements, and we may not generate significant product revenues or revenue from collaboration agreements, including our license and commercialization agreement with Eurofarma, or any income from operations. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments or competitive products;
- the prevalence and severity of any side effects;
- the ability to offer our product candidates for sale at competitive prices, including in the case of ridinilazole, which we expect, if approved, will compete with the antibiotics vancomycin and metronidazole, both of which are available in generic form at low prices, and fidaxomicin, and potentially other approaches to be used as an adjunctive therapy to antibiotics, such as the monoclonal antibody bezlotoxumab, vaccines or fecal biotherapy;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the timing of any such marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on concomitant use of other medications.

The ability to negotiate, secure and maintain third-party coverage and reimbursement may be affected by political, economic and regulatory developments in the United States, the European Union and other jurisdictions.

Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of ridinilazole or any of our other product candidates that receive marketing approval.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing a product candidate if and when such product candidates are approved.

We do not have a sales or marketing infrastructure and have no experience as a company in the sale or marketing of pharmaceutical products, although certain employees do have experience in the sale and marketing of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If ridinilazole receives marketing approval, we intend to seek commercialization partners in the United States and around the world. We will rely on Eurofarma to commercialize ridinilazole in Argentina,

Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Dominican Republic, Uruguay and Venezuela, pursuant to the license and commercialization agreement we entered into with Eurofarma in December 2017. There are risks involved with establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Legal, Tax, Regulatory and Compliance Risks

Even if we are able to commercialize ridinilazole or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize ridinilazole or any other product candidate successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. and E.U. healthcare industries and elsewhere is cost containment.

Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products.

For example, under Medicare, hospitals are reimbursed under an inpatient prospective payment system. This pricing methodology provides a single payment amount to hospitals based on a given diagnosis-related group. As a result, with respect to Medicare reimbursement for services in the hospital inpatient setting, hospitals could have a financial incentive to use the least expensive drugs for the treatment of CDI, generic antibiotics, which may significantly impact our ability to charge a premium for ridinilazole. We cannot be sure that coverage and reimbursement will be available for ridinilazole or any other product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug. If reimbursement is not

available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to clinical trial participants or patients;
- loss of revenue;
- increased insurance costs; and
- the inability to commercialize any products that we may develop.

The insurance policies covering our clinical trials are subject to a per claim deductible. The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin commercializing ridinilazole or any other product candidate that receives marketing approval. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes.

Our operations currently, and may in the future, involve the use of hazardous and flammable materials, including chemicals and medical and biological materials, and produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials or disposal of hazardous wastes, we could be held liable for any resulting damages, and any liability could exceed our resources.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on specific product candidates. As a result, we may forego or delay pursuit of opportunities with other product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates may not yield any commercially viable products. For example, in September 2020, following the review of data from preclinical studies, we determined to cease work on our gonorrhoeae program.

We have based our research and development efforts for CDI on the antibiotic ridinilazole. Notwithstanding our large investment to date and anticipated future expenditures in proprietary technologies that we use in the discovery of product candidates for CDI and other infectious diseases, we have not yet developed, and may never successfully develop, any marketed drugs. As a result of pursuing the development of product candidates using our proprietary technologies, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

The long-term effects of the United Kingdom's withdrawal from the European Union are not yet known and this uncertainty creates challenges and risks which make it more difficult for us to do business in Europe, which could adversely impact the market price of our common stock.

The United Kingdom formally withdrew from the European Union on January 1, 2020, commonly referred to as "Brexit." As a result, the United Kingdom is no longer part of the European Single Market and European Union Customs Union effective January 1, 2021. The future effects of Brexit are uncertain and will depend on the implementation of the Trade and Cooperation Agreement between the United Kingdom and the European Union ("TCA") and any other future agreements the United Kingdom may make to retain access to European Union markets. Under the TCA, which became effective on May 1, 2021, there is no longer free movement of goods or people between the United Kingdom and the European Union, which has resulted and could continue to result in certain delays in the shipment of goods from the United Kingdom to the European Union. Brexit could also lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which European Union laws to replace or replicate. The long-term risks of Brexit include economic recessions in the United Kingdom or other European markets and currency instability for both the British pound sterling and the euro. In the near term, there is a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective United Kingdom and European Union customs agencies that may delay time-sensitive shipments and may negatively impact our clinical trial supply chain, which includes locations in both the United Kingdom and the European Union.

Recent and potential future changes to U.S. and non-U.S. tax laws could materially adversely affect our company and holders of our shares of common stock.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or the TCJA, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act.

Future changes in tax laws, regulations and treaties, or the interpretation thereof, in addition to initiatives related to the Base Erosion and Profit Shifting, or BEPS, Project of the Organisation for Economic Co-Operation and Development, or OECD; the European Commission's "state aid" investigations; and other developments could have an adverse effect on the taxation of international businesses, including our own. Furthermore, countries where we are subject to taxes, including the United States, evaluate their tax policies and rules on a regular basis, and we may see significant changes in legislation and regulations concerning taxation.

We are unable to predict what tax changes may be enacted in the future or what effect such changes would have on our business, but such changes could affect our effective tax rates in countries where we have operations and could have an adverse effect on our overall tax position in the future, along with increasing the complexity, burden and cost of tax compliance.

Laws and regulations affecting government contracts, including our BARDA contract, make it more costly and difficult for us to successfully conduct our business. Failure to comply with these laws and regulations could result in significant civil and criminal penalties and adversely affect our business.

We must comply with numerous laws and regulations relating to the administration and performance of our government contracts, including our BARDA contract. Among the most significant government contracting regulations are:

- the Federal Acquisition Regulation, or FAR, and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;
- extensive U.S. government regulation of government-funded clinical research activities, including, for example, compliance requirements relating to protection of human and animal research subjects, restrictions on uses of human research materials, and conditions on dissemination of research results;
- business ethics and public integrity obligations, which govern areas such as conflicts of interest, the recruitment and hiring of former government employees, bribes and gratuities, and limitations on and mandatory disclosure of lobbying activities, pursuant to laws such as the Anti-Kickback Act, the Procurement Integrity Act, the False Claims Act and the Foreign Corrupt Practices Act; and
- export control and import laws and regulations.

In addition, U.S. government agencies such as the Department of Health and Human Services and the Defense Contract Audit Agency routinely audit and investigate government contractors for compliance with applicable laws and standards. These agencies review a contractor's performance under its contracts, cost structure and compliance with applicable laws, regulations and standards.

These agencies also review the adequacy of, and a contractor's compliance with, its internal control systems and policies, including the contractor's purchasing, property, estimating, compensation and management information systems. Any costs found to be unreasonable, unallowable under applicable reimbursement policies, or improperly allocated to a specific contract will not be paid, while such costs already paid must be refunded. Claims for costs that are expressly unallowable under applicable reimbursement policies may also be subject to administrative penalties. If we are audited and such audit uncovers improper or illegal activities, we may be subject to civil and criminal penalties and administrative sanctions, including:

- termination of any government contracts, including our BARDA contract;
- suspension of payments;
- administrative sanctions, such as long-term monitoring arrangements;
- fines; and
- suspension, debarment, or exclusion from eligibility for U.S. government contracts, funding programs and regulatory approvals.

In addition, we could suffer serious reputational harm if allegations of impropriety were made against us, which could jeopardize our other research programs, deter research institutions from engaging with us, and cause our stock price to decrease.

Even if we complete the necessary clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, including ridinilazole, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us or our collaborators from commercializing the product candidate. We have not received approval to market ridinilazole or any other product candidate from regulatory authorities in any jurisdiction.

We have only limited experience in filing and supporting the applications necessary to obtain marketing approvals for product candidates and expect to rely on third-party contract research organizations to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that ridinilazole or any of our other product candidates are not effective or only moderately effective, or have undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing approval or that prevent or limit commercial use.

The process of obtaining marketing approvals is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in these other jurisdictions, and any approval we are granted for our product candidates in the United States and Europe would not assure approval of our product candidates in other jurisdictions.

In order to market and sell ridinilazole and our other product candidates in foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements in those jurisdictions. The approval

procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA or EMA approval. The regulatory approval process outside the United States and Europe generally includes all of the risks associated with obtaining FDA and EMA approval. In addition, some countries outside the United States and Europe require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement. We may not obtain marketing, pricing or reimbursement approvals outside the United States and Europe on a timely basis, if at all. Approval by the FDA or the EMA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States and Europe does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA or the EMA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Marketing approvals in countries outside the United States and Europe do not ensure pricing approvals in those countries or in any other countries, and marketing approvals and pricing approvals do not ensure that reimbursement will be obtained.

Our ability to obtain and maintain conditional marketing authorizations in the European Union is limited to specific circumstances and subject to several conditions and obligations. A failure to renew any conditional approval that we obtain prior to full approval for the applicable indication would prevent us from continuing to market our products.

Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under E.U. law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions. Even if we, or a third-party collaborator, obtain conditional approval for ridinilazole for the treatment of CDI, or any other product candidate, we or they may not be able to renew such conditional approval.

Even if we obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, including the requirement to implement a risk evaluation and mitigation strategy or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We and our collaborators must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, neither we nor our collaborators will be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to ensure that quality control and manufacturing procedures conform to cGMP, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMP.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding

maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice, or DOJ, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of such requirements may lead to investigations alleging violations of the Food, Drug and Cosmetic Act and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical need for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has granted fast track designation for ridinilazole. However, a fast-track designation does not ensure that ridinilazole will receive marketing approval or that approval will be granted within any particular timeframe. We may also seek fast track designation for other product candidates. Even if the FDA grants fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of our product candidates.

If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. Because the FDA

designated ridinilazole as a qualified infectious disease product, or QIDP, ridinilazole will receive priority review. We may also request priority review for other product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

Our relationships with customers, healthcare providers and professionals and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates, including ridinilazole, for which we obtain marketing approval. Our future arrangements with customers, healthcare providers and professionals and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, and are not limited to, the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations.
- The federal False Claims Act imposes civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and qui tam relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government. There is also a separate false claims provision imposing criminal penalties.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.
- HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal Physician Sunshine Act requirements under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, referred to together as the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value made to or at the request of covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests in such manufacturers. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from

government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Exclusion, suspension and debarment from government funded healthcare programs would significantly impact our ability to commercialize, sell or distribute any drug. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% as of January 1, 2019) point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2029 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to revise or replace elements of the ACA during the next Congressional session, whether in response to pending high court decisions or at its own initiative to amend or supplement the ACA. It is unclear how ongoing litigation

and other efforts to amend the ACA will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

The costs of prescription pharmaceuticals has also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, the Trump administration's budget proposal for fiscal year 2021 had included a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. It remains unclear the extent which the Biden administration and the new session of Congress will seek new legislative and/or administrative measures to control drug costs.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the U.K. Bribery Act 2010, or Bribery Act, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA, Bribery Act and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, Bribery Act or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States and the United Kingdom, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA, the Bribery Act and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control laws by U.S., U.K. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Risks Related to Our Intellectual Property, Cybersecurity and Data Privacy

If we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of our patent protection is not sufficiently broad, our competitors could develop and commercialize technology and drug products similar or identical to ours, and our ability to successfully commercialize our technology and drug product candidates may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products, including our Discuva Platform. We seek to protect our proprietary position by filing patent applications in the United States, in Europe and in certain additional foreign jurisdictions related to our novel technologies and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we license technology or product candidates from third parties in the future, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering the licensed technology or product candidates. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted or enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents, narrow the scope of our patent protection or make enforcement more difficult or uncertain.

The laws of foreign countries may not protect our patent rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, for the foregoing reasons, we may not pursue or obtain patent protection in all major markets or may not obtain protection that enables us to prevent the entry of third parties into the market.

Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our U.S. patents or pending U.S. patent applications, or that we were the first to file for patent protection of such inventions outside the United States or, since March 16, 2013, within the United States.

Moreover, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, reissue, inter parties review, post grant review, interference proceedings or other patent office proceedings, court litigation or International Trade Commission proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation concerning our patent rights could reduce the scope of or prevent the enforceability of, or invalidate, our patent rights, allowing third parties to commercialize our technology or products, or equivalent or similar technology or products, and so to compete directly with us, without payment to us, or, where such proceedings involve third-party patents, result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened or narrowed by operation of any of the foregoing, such an event could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Competitors may have filed patent applications or received patents and may obtain additional patents and proprietary rights that block or compete with our patents. This could require us to design around the claims of patents covering our products that may have been issued by our competitors or obtain a license, either of which would could cause us to incur additional expenses. We may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property. Even if our patent applications issue as patents, they may not issue in a form that will provide us with adequate protection to prevent competitors from competing with us or otherwise to provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar, improved or alternative technologies or products in a non-infringing manner.

For example, although ridinilazole is protected by a U.S. composition of matter patent that recites hydrated forms of ridinilazole, and a method of treatment patent for *Clostridioides difficile* associated disease, patent protection is not available for composition-of-matter claims that only recite the active pharmaceutical ingredient for ridinilazole without limitation to its use. Because ridinilazole lacks composition-of-matter protection for its active pharmaceutical ingredient, competitors will, subject to obtaining marketing approval, be able to offer and sell products with the same active pharmaceutical ingredient so long as these competitors do not infringe any other issued patents that would otherwise cover the drug's usage, methods of treatment using the drug, drug formulations, drug dosage forms and the like. Moreover, method-of-treatment patent claims are more difficult to enforce than composition-of-matter claims for reasons including off-label sale, potential divided infringement issues and use of the subject compound in non-infringing manners. Physicians are permitted to prescribe an approved product for uses that are not described in the product's labeling. Although off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. Off-label sales would limit our ability to generate revenue from the sale of our product candidates, if approved for commercial sale. In addition, if a third party were able to design around our dosage-form and formulation patents and create a different formulation and dosage form that is not covered by our patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity, such as orphan drug exclusivity in the United States, which we obtain under applicable legislation, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the European Union and elsewhere may also result in clinical trial data submitted as part of a marketing authorization application becoming publicly available. Such developments could enable other companies to use our clinical trial data to assist in their own product development and to obtain marketing authorizations in the European Union and in other jurisdictions. Such developments may also require us to allocate significant resources to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Future changes in U.S. statutory or case law beyond our control could affect some or all of the foregoing possibilities. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. This could be the case even after giving effect to patent term extensions and data exclusivity provisions preventing third parties from relying on clinical trial data filed by us for regulatory approval in support of their own applications for such approval. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits or other enforcement proceedings to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and potentially unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property or that our patent and other intellectual property rights are invalid or unenforceable, including for anti-trust reasons. As a result, in a patent infringement proceeding, a court or administrative body may decide that a patent of ours is invalid or unenforceable, in whole or in part, or may construe the patent's claims narrowly and so refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the competitor technology in question. Even if we are successful in a patent infringement action, the unsuccessful party may subsequently raise antitrust issues and bring a follow-on action thereon. Antitrust issues may also provide a bar to settlement or constrain the permissible settlement terms. Further, settlement agreements in the pharmaceutical sector are the subject of ongoing review by the antitrust authorities in the European Union.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies, including our Discuva Platform, without infringing the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, inter parties review, reexamination, reissue or post-grant review proceedings before the USPTO. The risks of being involved in such litigation and office proceedings may also increase as our product candidates approach commercialization, and as we gain greater visibility as a publicly traded company in the United States. Third parties may assert infringement claims against us based on existing or future intellectual property rights and so restrict our freedom to operate. Third parties may also seek injunctive relief against us, whereby they would attempt to prevent us from practicing our technologies altogether pending outcome of any litigation against us.

If we are found to infringe a third party's intellectual property rights, or in order to avoid or settle litigation, we could be required to obtain a license to enable us to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies as are licensed to us, and could require us to make substantial payments. Absent a license, we could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties, or claims that we derived our inventions from another, could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary or otherwise confidential information or know-how of others in their work for us, we may be subject to claims that we or these employees have without authorization used or disclosed intellectual property, including trade secrets or other proprietary or confidential information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us and agreeing to cooperate and assist us with securing and defending our intellectual property, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our shares of common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Accordingly, costs and lost management time, as well as uncertainties resulting from the initiation and continuation of patent litigation or other proceedings, could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary and confidential information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary or confidential information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets, particularly unpatented know-how, were to be obtained or independently developed by a competitor, our competitive position would be harmed.

We are exposed to risks related to cybersecurity threats, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our computer systems and those of third parties with whom we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liabilities and the further development of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

While we have not experienced any material losses relating to cyber-attacks, we have been the subject of cyber-attacks. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information in order to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. While we continue to assess and address the implications of existing and new domestic and foreign regulations relating to data privacy, the evolving regulatory landscape presents a number of legal and operational challenges, and our efforts to comply with these regulations may be unsuccessful. For example, European Union ("EU") regulations have established a prohibition on the transfer of personally identifiable information from the EU to other countries whose laws do not protect personal data to an adequate level of privacy or security. While we have utilized certain permitted approaches for transferring personally identifiable information from the EU to the United States, these approaches may be reviewed and invalidated by EU courts or regulatory bodies and we may be required to ascertain an alternative legal basis for such transfers. Additionally, we may also face audits or investigations by one or more government agencies relating to our compliance with these regulations that could result in the imposition of penalties or fines, significant expenses in facilitating and responding to the investigations, and overall reputational harm or

negative publicity. The costs of compliance with, and other burdens imposed by, these laws, regulations and policies including, restrictions on marketing activities, could have a material adverse effect on our business, financial condition and operating results.

Risks Related to Corporate Governance and Employee Relations

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our executive and scientific teams, including Robert W. Duggan, our Chief Executive Officer, and Dr. Mahkam Zanganeh, our Chief Operations Officer. Although we have formal employment agreements with some of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain "key person" insurance on any of our executive officers. The unplanned loss of the services of any of these persons could materially impact the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel, including in the United States where we plan to continue to expand our physical presence, will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous biotechnology and pharmaceutical companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our principal stockholder and chief executive officer maintains the ability to control or significantly influence all matters submitted to stockholders for approval.

As of December 31, 2021, Mr. Duggan beneficially owned, in the aggregate, shares of common stock representing approximately 70% of our outstanding capital stock. Mr. Duggan is able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, Mr. Duggan is able to control or influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire. As a member of the board of directors, Mr. Duggan will adhere to the corporate governance standards adopted by the company.

As a "controlled company" under the listing requirements of the Nasdaq Stock Market, we have an exemption from certain corporate governance requirements, which could adversely affect our stockholders by denying them certain rights and protections.

Mr. Duggan owns more than a majority of the voting power of our outstanding shares of common stock. Under the Nasdaq Stock Market listing requirements, a company of which more than 50% of the voting power is held by an individual, group, or another company is a "controlled company." We have in the past, and we expect in the future, to rely on the "controlled company" exemptions under the Nasdaq Stock Market listing requirements. For example, in the past, a majority of the members of our board of directors were not independent directors, and our compensation and nominating and corporate governance committees did not consist entirely of independent directors. Accordingly, during the period we remain a controlled company and during any transition period following a time when we are no longer a controlled company, you may not have the same protections afforded to stockholders of companies that are subject to all of the corporate governance requirements of the Nasdaq Stock Market.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA or Office of Inspector General regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Similar employee fraud or misconduct could occur with respect to reimbursement requests and other reports we are required to submit to BARDA. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation, or a request for the reimbursement of expenses that were not incurred, which could cause BARDA to terminate our

contract with them. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Owning Our Common Stock

The prices of our shares of common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

The market prices of our shares of common stock on the Nasdaq Global Market may be volatile and fluctuate substantially. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, stockholders may not be able to sell their shares of common stock at or above the price at which they were purchased.

The market price for our shares of common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of ridinilazole and any other product candidate that we develop;
- results of clinical trials of product candidates of our competitors;
- changes or developments in laws or regulations applicable to ridinilazole and any other product candidates that we develop;
- our entry into, and the success of, any collaboration agreements with third parties;
- the operation of our contract with BARDA, and whether BARDA elects to pursue its remaining option work segment beyond the base period;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates, products or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the biotechnology and pharmaceutical sectors;
- regulatory or legal developments in the United States and other countries;
- the societal and economic impact of public health epidemics, such as the ongoing COVID-19 pandemic, and government efforts to slow their spread;
- general economic, industry and market conditions;
- the trading volume of the shares on the Nasdaq Global Market; and
- the other factors described in this “Risk Factors” section.

Our shares of common stock do not trade on any exchange outside of the United States.

Our shares of common stock are listed only in the United States on The Nasdaq Global Market, and we have no plans to list our shares in any other jurisdiction. As a result, a holder of our shares of common stock outside of the United States may not be able to effect transactions in our shares as readily as the holder may if our shares were listed on an exchange in that holder’s home jurisdiction.

Substantial future sales of our shares of common stock in the public market, or the perception that these sales could occur, could cause the price of the shares to decline significantly, even if our business is doing well.

Sales of a substantial number of our shares of common stock in the public market could occur at any time. These sales, or the perception in the market that these sales could occur, could cause the market price of the shares to decline. Following the domestication, all of our outstanding shares of common stock were freely tradeable in the public market without restriction, unless held by our affiliates. Our principal stockholder and chief executive officer, Mr. Robert W. Duggan, holds a substantial

number of shares. Mr. Duggan's shares have been registered for resale pursuant to an effective registration statement on Form S-3. If he sells, or indicates an intention to sell, substantial amounts of shares in the public market, the trading price of our shares could decline.

We are a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our shares of common stock less attractive to investors.

We are a "smaller reporting company," as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended. We would cease to be a smaller reporting company if we have a public float in excess of $250 million or have annual revenues in excess of $100 million and a public float in excess of $700 million, determined on an annual basis.

We expect to continue to take advantage of some or all of the exemptions available to us as a smaller reporting company. We cannot predict whether investors will find our shares of common stock less attractive if we rely on these exemptions. If some investors find our shares of common stock less attractive as a result, there may be a less active trading market for the shares and the market price of the shares may be more volatile.

We incur increased costs as a result of operating as a company with shares of common stock that are publicly traded in the United States, and our management is required to devote substantial time to compliance initiatives.

As a company with shares of common stock that are publicly traded in the United States, and particularly after we are no longer a "smaller reporting company," we have incurred and will continue to incur significant legal, accounting and other expenses that we did not previously incur. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Act, the listing requirements of the Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

However, for as long as we remain a smaller reporting company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not smaller reporting companies as described in the preceding risk factor.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our shares of common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our shares of common stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis, and our management is required to assess the effectiveness of these controls annually. However, for as long as we are a "smaller reporting company", our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. Pursuant to Section 404(a) of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal controls over financial reporting. In order to comply with Section 404(a) of the Sarbanes-Oxley Act, we expect to incur additional expenses and devote increased management effort including documenting and evaluating our internal controls over financial reporting. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware and the federal district courts of the United States of America as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers and employees.

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders;
- any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or
- any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find the either exclusive forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and operating results.

Because we do not anticipate paying any cash dividends on our shares of common stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our shares of common stock or on Summit Therapeutics plc's ordinary shares. We currently intend to retain all of our future earnings to fund the development and expansion of our business. Any determination to pay dividends in the future will be at the discretion of our board of directors. As a result, capital appreciation of our shares of common stock, if any, will be the sole source of gain for our stockholders for the foreseeable future.

If equity research analysts stop publishing research or reports about our business or if they issue unfavorable commentary or downgrade our shares of common stock, the price of the shares could decline.

The trading market for our shares of common stock relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of our shares of common stock could decline if one or more equity research analysts downgrades such securities or if analysts issue other unfavorable commentary about us or our business. In addition, if one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause the trading prices and trading volumes of our shares of common stock to decline.

We are exposed to risks related to currency exchange rates.

We conduct a significant portion of our operations in the United Kingdom. Because our financial statements are presented in U.S. dollars, changes in currency exchange rates have had and could have a significant effect on our operating results when our operating results are translated into pounds sterling. Exchange rate fluctuations between local currencies and the U.S. dollar

create risk in several ways, including the following: weakening of the U.S. dollar may increase the U.S. dollar cost of overseas research and development expenses and the cost of sourced product components outside the United Kingdom; strengthening of the U.S. dollar may decrease the value of our revenues denominated in other currencies; the exchange rates on non-dollar transactions and cash deposits can distort our financial results; and commercial pricing and profit margins are affected by currency fluctuations.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion in the use of our cash and cash equivalents and could spend our cash in ways that do not improve our results of operations or enhance the value of our shares of common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the market price of our shares of common stock to decline and delay the development of our product candidates.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

The following table provides information concerning Summit's principal leased facilities as of December 31, 2021:

We maintain the following leased properties:

Type/Uses	Location	Size	Lease Expiration
Executive office	Oxfordshire, United Kingdom	6,781 square feet	February 2027
Executive office	Cambridge, Massachusetts, United States	996 square feet	Rolling
Executive office	Menlo Park, California, United States	4,500 square feet	September 2022
Laboratory and office	Sawston, United Kingdom	7,644 square feet	October 2026

We believe our facilities are suitable and adequate to meet our needs.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock has been publicly traded on the Nasdaq Global Market under the symbol “SMMT” since September 21, 2020. Prior to that date, there was no public market for our common stock. Prior to the closing of the Redomiciliation Transaction, pursuant to which Summit Therapeutics plc became our wholly-owned subsidiary, Summit Therapeutics plc's American Depositary Shares, (or "ADSs"), had traded on the Nasdaq Global Market under the symbol "SMMT" since March 2015. Each ADS represented five ordinary shares of Summit Therapeutics plc. In the Redomiciliation Transaction, five ordinary shares of Summit Therapeutics plc were exchanged for one share of our common stock. The ordinary shares of Summit Therapeutics plc previously traded on AIM, a sub-market of the London Stock Exchange plc ("AIM"), under the symbol “SUMM.” We canceled the admission of the ordinary shares to trading on AIM on February 24, 2020.

Holders of Record

As of March 10, 2022, there were approximately 323 holders of record of our common stock. The actual number of stockholders is greater than this number of holders of record and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid cash dividends on our common stock or ordinary shares. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our Board of Directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects, and other factors our Board of Directors may deem relevant.

Recent Sales of Unregistered Securities

On December 24, 2019, in connection with the closing of a private placement for an aggregate purchase price of $50 million in cash, we issued an aggregate of 35,075,690 shares of common stock to investors, of which 33,231,410 shares of common stock were subscribed by Mr. Robert W. Duggan. These shares were sold to each investor at a price of $1.43 per share of common stock. The common stock was offered and sold pursuant to an exemption from the registration requirements under Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated thereunder.

On July 17, 2020, in connection with our incorporation, we issued an aggregate of 100 shares of our common stock to a nominee stockholder for $1.00. The shares were offered and issued pursuant to Section 4(2) of the Securities Act of 1933, as amended, or the "Securities Act".

On September 18, 2020, we issued an aggregate of 67,231,903 shares of our common stock in exchange for the entire issued share capital of Summit Therapeutics plc in a transaction exempt from registration pursuant to Section 3(a)(10) of the Securities Act. No cash was paid for these shares.

On November 6, 2020, in connection with the closing of a private placement for an aggregate purchase price of $50 million in cash, we issued an aggregate of 14,970,060 shares of our common stock to three investors: our Chief Executive Officer Robert W. Duggan, the Mahkam Zanganeh Revocable Trust and Polar Capital Funds plc - Biotechnology Fund. The shares were sold to each of the foregoing investors at a price of $3.34 per share of common stock. The common stock was offered and sold pursuant to an exemption from the registration requirements under Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated thereunder.

On March 24, 2021, Mr. Duggan entered into a Note Purchase Agreement (the "Initial Purchase Agreement") pursuant to which he loaned the Company $55.0 million in exchange for the issuance by the Company of an unsecured promissory note (the “Initial Note”) in the amount of $55.0 million. The Note accrues interest at a rate per annum equal to 150% of the applicable 10 Year US Treasury rate, as adjusted monthly. The rate is initially estimated to be approximately 2.4%. The Company may prepay any portion of the Note at its option without penalty. The Note will mature and become due upon the earlier of (i) the consummation of a registered public offering with net proceeds of no less than $55.0 million, or (ii) 13 months from the date of issuance of the Note. The Note was issued to Mr. Duggan in a private placement in reliance Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated thereunder. On April 20, 2021, the Company determined, with Mr. Duggan’s agreement, to rescind both the Initial Purchase Agreement and the Initial Note issued thereunder, and repaid the principal amount of the Initial Note in full, without interest or penalty, as such the Company recognized imputed interest of $0.1 million within additional paid in capital.

On April 20, 2021, subsequent to the repayment of the Initial Note, Mr. Duggan entered into a second Note Purchase Agreement (the “Second Purchase Agreement”) pursuant to which he loaned the Company $55.0 million in exchange for the issuance by the Company of an unsecured promissory note (the “Second Note”) in the amount of $55.0 million. The Second Note accrued interest at a rate per annum equal to 150% of the applicable 10 Year US Treasury rate, as adjusted monthly (initially estimated to be approximately 2.4%). The Company was permitted to prepay any portion of the Second Note at its option without penalty. Pursuant to the terms of the Second Note, following consummation of the rights offering the Second Note matured and all principal and interest thereunder was repaid by the Company using a portion of the proceeds of the rights offering.

On March 10, 2022, the Company’s Chief Executive Officer, Robert W. Duggan, entered into a Note Purchase Agreement (the “2022 Note”), pursuant to which he has loaned the Company $25.0 million in exchange for the issuance by the Company of an unsecured promissory note in the amount of $25.0 million. The 2022 Note is to accrue interest at a rate per annum equal to the prime rate as reported in the *Wall Street Journal*, which is 3.25% as of the effective date. The 2022 Note becomes due upon the earlier of (i) the consummation of a registered public offering with net proceeds of no less than $25.0 million or (ii) 18 months from the date of issuance of the 2022 Note.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. Selected Financial Data

Reserved.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in “Item 1A. Risk Factors” of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

The Management's Discussion and Analysis of Financial Condition and Results of Operations, or MD&A, describes principal factors affecting the results of our operations, financial condition and liquidity, as well as our critical accounting policies and estimates that require significant judgment and thus have the most significant potential impact on our Consolidated Financial Statements. This section provides an analysis of our financial results for the year ended December 31, 2021 compared to the year ended December 31, 2020. For the discussion and analysis covering the year ended December 31, 2020 compared to the eleven months ended December 31, 2019, please refer to "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on March 31, 2021.

Company Overview

We are a biopharmaceutical company focused on the discovery, development, and commercialization of patient-, physician-, caregiver- and societal-friendly medicinal therapies intended to improve quality of life, increase life expectancy, and resolve

serious unmet needs. Our novel mechanism pipeline of product candidates is designed with the goal to become the patient-friendly, new-era standard-of-care medicines, and to work in harmony with the human microbiome. Summit's lead product candidate, ridinilazole, is a novel first-in-class drug that is engaged in a global Phase III clinical trial program. On December 20, 2021, we announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole for treating patients suffering from *Clostridioides difficile* infection, also known as *C. difficile* infection, or CDI. Our second product candidate, SMT-738, was announced in May 2021 for combating multidrug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. SMT-738 is the first of a novel class of precision antibiotics that has entered into preclinical development. We intend to expand our portfolio by developing further new mechanism, new era product offerings that are designed to work in harmony with the human gut microbiome in the therapeutic areas of oncology and infectious diseases.

To date, we have financed our operations primarily through issuances of our common stock (and before the Redomiciliation Transaction (as defined below) issuances of Summit Therapeutics plc's ordinary shares and American Depositary Shares, or ADSs), payments to us under our license and commercialization agreement with Eurofarma Laboratórios SA, or Eurofarma, development funding and other assistance from government entities, philanthropic, non-government and not-for-profit organizations for our product candidates. In particular, we have received funding from BARDA, CARB-X, Innovate UK, Wellcome Trust and a number of not-for-profit organizations.

We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed the development of any drugs. We expect to continue to incur significant expenses and increasing operating losses for at least the next few years. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, due to the nature and timing of our research and development activities. We expect that our research and development and general and administrative expenses will continue to be significant in connection with our ongoing research and development efforts. In addition, if we obtain marketing approval of ridinilazole in the U.S. or other jurisdictions where we retain commercial rights, and if we choose to maintain those rights, we would expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses, as well as ongoing research and development expenses.

Recent Developments

On May 12, 2021, we closed our rights offering, which was fully subscribed. We received aggregate gross proceeds from the rights offering of $75.0 million from the sale of 14,312,976 shares of our common stock at a price per share of $5.24. Issuance costs associated with the rights offering were immaterial. In connection with the closing of the rights offering, a promissory note, dated April 20, 2021, issued by us in favor of our Chairman, Chief Executive Officer, and the beneficial owner of approximately 70% of our outstanding common stock prior to this rights offering, Robert W. Duggan, in the principal amount of $55.0 million, matured and became due and we repaid all principal and accrued interest thereunder using a portion of the proceeds from the rights offering.

On August 11, 2021, based on a thorough review of the design and enrollment status of its two ongoing blinded Phase III Ri-CoDIFy trials, we announced that we combined our two blinded pivotal Phase III clinical trials evaluating ridinilazole versus vancomycin into a single study and presented this decision to the United States ("U.S.") Food and Drug Administration (the "FDA") as such. During September 2021, we received feedback from the FDA that the FDA did not agree with the change to the primary endpoint that we proposed and subsequently implemented in our ongoing Phase III Ri-CoDIFy studies when combining the trials.

On December 20, 2021 we announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole, for the treatment of and Sustained Clinical Response ("SCR"), as defined below, for patients suffering from *C. difficile* infection ("*C. diff.* infection" or "CDI"). The study showed that ridinilazole resulted in a numerically higher SCR rate than vancomycin, but did not meet the study's primary endpoint for superiority. The pivotal Phase III clinical trial consisted of two Phase III clinical trials combined into a single study, designed to assess, as the primary endpoint, the superiority of ridinilazole compared to vancomycin in SCR, which is defined as Clinical Response of the treated episode of CDI and no recurrence of CDI through 30 days after the end of treatment. Additional endpoints include Clinical Response ("CR"), safety, tolerability, recurrence, and analyses of the gut microbiome and metabolome, in addition to quality of life and health economic outcome measures. We are in the process of evaluating the future path forward with respect to ridinilazole, including potential partnership opportunities.

Key Components of our Results of Operations

Revenue

Revenue consists of amounts received from the license and commercialization agreement with Eurofarma Laboratórios S.A. ("Eurofarma"). We have not generated any revenue from product sales.

Under the terms of the license and commercialization agreement with Eurofarma, we received an upfront payment of $2.5 million in December 2017. In February 2020, we achieved the first enrollment milestone and received $1.0 million. In September 2021, we achieved the second enrollment milestone and received $1.3 million. The terms of the contract have been assessed under ASC 606 and currently only the upfront payment and the first two milestone payments are included in the transaction price. These payments were initially reported as deferred revenue in the balance sheet and are being recognized as revenue ratably over the performance period.

Revenue recognized during the period ended December 31, 2021 related to the upfront payment and the first two enrollment milestones earned in accordance with our revenue recognition policy. Revenue recognized during the period ended December 31, 2020 related to the upfront payment and the first enrollment milestone earned in accordance with our revenue recognition policy. The revenue is being recognized ratably over the performance period to reflect the transfer of control to the customer occurring over the time period that the research and development services are provided. This output method is, in management's judgment, the best measure of progress towards satisfying the performance period.

In addition, we will be entitled to receive an additional $1.5 million for achieving various development milestones. We are also eligible to receive up to $21.4 million in additional development, commercial and sales milestones when cumulative net sales equal or exceed $100.0 million in the Eurofarma licensed territory. For each incremental $100.0 million in cumulative net sales achieved, we are entitled to additional milestone payments, which, when combined with the aforementioned anticipated product supply transfer payments, is estimated to range from a mid-teens to high-teens percentage of cumulative net sales in the territories where we have granted Eurofarma commercialization rights.

Other Operating Income

Other operating income includes income received and recognized from grants and clinical trial support from government entities, philanthropic, non-government and not-for-profit organizations. In September 2017, we were awarded a funding contract from the Biomedical Advanced Research and Development Authority ("BARDA"), part of the Office of the Assistant Secretary for Preparedness and Response at the United States Department of Health and Human Services, in support of our Ri-CoDIFy clinical trials and clinical development of ridinilazole. The awarded contract was originally worth up to $62.0 million. In June 2019 and again in January 2020, BARDA increased the value of the contract such that it is now worth up to $72.5 million. The remaining federal government funding is dependent on BARDA in its sole discretion exercising the final independent option work segment, upon the achievement by the Company of certain agreed-upon milestones for ridinilazole. As of December 31, 2021, an aggregate of $56.5 million of the total committed BARDA funding had been received and the Company has recognized $50.3 million of cumulative income since contract inception.

We have also received income from research and development ("R&D") tax credits, which consist of the R&D tax credit received in the United Kingdom ("U.K."). We benefit from two U.K. research and development tax credit cash rebate regimes: Small and Medium Enterprise Program ("SME Program") and the Research and Development Expenditure Credit Program ("RDEC Program"). Qualifying expenditures largely comprise employment costs for research staff, consumables, a proportion of relevant, permitted sub-contract costs and certain internal overhead costs incurred as part of research projects for which we do not receive income. Tax credits related to the SME Program and RDEC Program are recorded as other operating income in the consolidated statements of operations and other comprehensive loss. Under both schemes, we receive cash payments that are not dependent on our pre-tax net income levels.

Based on criteria established by Her Majesty's Revenue and Customs ("HMRC"), a portion of expenditures being carried out in relation to our pipeline research and development, clinical trials management and third-party manufacturing development activities are eligible for the SME regime and we expect such elements of expenditure will also continue to be eligible for the SME regime for future periods.

In May 2021, we announced the selection of a new preclinical candidate, SMT-738, from the DDS-04 series for development in the fight against multi-drug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. Simultaneously, we received an award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program ("CARB-X") to progress this candidate through preclinical development and

Phase Ia clinical trials. The award commits initial funding of up to $4.1 million with the possibility of up to another $3.7 million based on the achievement of future milestones. As of December 31, 2021, $0.5 million of grant funding from CARB-X has been received and the Company has recognized $1.2 million of cumulative income since contract inception.

Operating Expenses

The majority of our operating expenses since inception have consisted of research and development activities and general and administrative costs.

Research and Development Expenses

Research and development expenses consist of all costs associated with our research and development activities.

These include:

- costs incurred in conducting our preclinical studies and clinical trials through contract research organizations, including preclinical toxicology, pharmacology, formulation and manufacturing work;
- laboratory and vendor expenses incurred in relation to our preclinical and non-clinical studies;
- costs incurred in supply chain development and scale up activities to support product registration;
- employee related expenses, which include salary, benefits and stock-based compensation, for our research and development staff; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

We utilize our employee and infrastructure resources across multiple research projects. We track expenses related to our clinical programs and certain preclinical programs on a per project basis. We expect our research and development expenses to continue to be significant as we continue our early-stage research programs for the treatment of Enterobacteriaceae infections, continue our activities to initiate preclinical programs for future product candidates, including under our Discuva Platform, and develop product candidates that we may obtain through business development activities. The timing and amount of these expenses will depend upon the outcome of our clinical trials and the associated costs. The timing and amount of these expenses will also depend on the costs associated with potential future clinical trials of our product candidates and the related expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs and product candidate manufacturing costs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and benefits related to our executive, finance, business development, human resources and other support functions. Other general and administrative expenses include stock-based compensation expenses, market research costs, facility-related costs, consulting costs and expenses associated with the requirements of being a publicly traded company in the United States, including insurance, legal, audit and taxation services fees.

We anticipate that our general and administrative expenses will continue to increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also anticipate continued accounting, audit, regulatory, compliance, insurance and investor and public relations expenses associated with being a publicly traded company in the United States. Prior to the Redomiciliation Transaction, our American Depositary Shares, or ADSs, had traded on the Nasdaq Global Market and, until we canceled the admission on February 24, 2020, our ordinary shares had traded on the Alternative Investment Market in the United Kingdom. Our common stock is currently traded on the Nasdaq Global Market, and therefore, we only anticipate incurring future expenses associated with being a listed public company in the United States.

Taxation

As a U.S. tax resident trading entity we are subject to U.S. corporate taxation. Prior to the Redomiciliation Transaction we were a U.K. resident trading entity and were subject to U.K. corporate taxation on group-wide taxable income. Our U.K. resident trading subsidiaries are still individually subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since inception. We have recorded a full valuation allowance against the deferred tax assets with respect to

these tax losses in excess of our deferred tax liabilities because we do not consider it probable that there will be suitable taxable profits in the foreseeable future based on the evidence available against which to offset these losses.

Jumpstart Our Business Startups Act of 2012

As of January 1, 2021, we are no longer an "emerging growth company" as defined in the Jumpstart our Business Startups Act of 2012, or the JOBS Act. Formerly, as an emerging growth company, we were able to take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. The last day of the fiscal year following the fifth anniversary of our initial public offering in March 2015 was December 31, 2020, hence we have ceased to be an emerging growth company.

Business Impact of COVID-19 Pandemic

The COVID-19 pandemic and measures taken to contain it have affected our business and operations in several ways. These include, but are not limited to, the following:

- A substantial portion of our employees are remote working. We have been unable to undertake certain activities directly at the same level as prior to the COVID-19 pandemic, including clinical trial visits and investigator meetings, with such activities being done remotely where possible. We have been relying on remote means of working and communication both internally and externally. We are continuing to monitor and support the health and well-being of our employees and their productivity as remote working continues.

- Certain of our clinical trial sites have suspended enrollment due to facility closures, reduced staff and operations, quarantine travel restrictions and other governmental restrictions. Additionally, we experienced patient enrollment at a slower pace than expected at certain clinical trial sites which resulted in increased clinical development costs.

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- Many of our clinical trial sites have been operating with reduced staff and other restrictions. We increased our efforts to engage with our clinical trial sites with a focus on retaining patients and maintaining scheduled visits and treatments, and where possible, instituted practices such as addition of home healthcare provider services for patients and remote monitoring.

The ongoing COVID-19 pandemic continues to evolve and its enduring impact on our business remains uncertain. There may be other material adverse impacts on our business, operations and financial condition that are unpredictable at this time, including delays in the development and regulatory approval of our product candidates and difficulties in retaining qualified personnel during the pandemic and once it subsides. The extent to which the pandemic may impact our business will depend on future developments, such as the duration of the pandemic, quarantines, travel restrictions and other measures in the U.S., the U.K. and around the world, business closures or business disruptions and the effectiveness of actions taken to contain the pandemic.

Results of Operations

Comparison of the Year Ended December 31, 2021 to the Year Ended December 31, 2020

(in millions)	Year Ended		Change 2021 vs. 2020
	December 31, 2021	December 31, 2020	Increase/(Decrease)
Revenue	$ 1.8	$ 0.9	$ 0.9
Operating expenses:			
Research and development	85.4	53.3	32.1
General and administrative	23.6	19.2	4.4
Impairment of intangible assets	—	0.9	(0.9)
Total operating expenses	109.0	73.4	35.6
Other operating income	21.0	19.3	1.7
Operating loss	(86.2)	(53.2)	(33.0)
Other (expense) income, net	(2.4)	0.3	(2.7)
Loss before income taxes	(88.6)	(52.9)	(35.7)
Income tax benefit	—	0.2	(0.2)
Net loss	$ (88.6)	$ (52.7)	$ (35.9)

Revenue

Revenue increased $0.9 million for the year ended December 31, 2021, compared to the same period in the prior year. The increase is primarily attributed to the achievement of a milestone related to our license and commercialization agreement with Eurofarma Laboratórios S.A. ("Eurofarma") in September of 2021. The total milestone of $1.3 million is recognized ratably over the performance period the research and development services are provided, which extends beyond 2021.

Operating Expenses

Research and Development Expenses

(in millions)	Year Ended		Change 2021 vs. 2020
	December 31, 2021	December 31, 2020	Increase/(Decrease)
CDI program	$ 53.9	$ 37.5	$ 16.4
Antibiotic pipeline research and development costs	1.9	1.8	0.1
Other research and development costs	29.6	14.0	15.6
Total	$ 85.4	$ 53.3	$ 32.1

Investment in our CDI program increased by $16.4 million for the year ended December 31, 2021, compared to the same period in the prior year, primarily due to clinical and manufacturing activities associated with the Phase III clinical program of ridinilazole.

Investment in our antibiotic pipeline development activities was $1.9 million for the year ended December 31, 2021, which reflects costs associated with development of our preclinical candidate, SMT-738, from the DDS-04 series for development in the fight against multi-drug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. Investment in our antibiotic pipeline development activities was $1.8 million for the year ended December 31, 2020, which reflects costs associated with work on the DDS-01 series and the gonorrhoeae program which we ceased work on at the end of 2020.

Other research and development costs are comprised of the following:

(in millions)	Year Ended		Change 2021 vs. 2020
	December 31, 2021	December 31, 2020	Increase/(Decrease)
Compensation related costs	$ 19.4	$ 10.0	$ 9.4
Stock-based compensation	5.9	0.3	5.6
Other research and development costs	4.3	3.7	0.6
Total	$ 29.6	$ 14.0	$ 15.6

Other research and development costs increased by $15.6 million for the year ended December 31, 2021, compared to the same period in the prior year, due primarily to an increase of $9.4 million in compensation related costs and an increase of $5.6 million in stock-based compensation as a result of increased hiring.

General and Administrative Expenses

(in millions)	Year Ended		Change 2021 vs. 2020
	December 31, 2021	December 31, 2020	Increase/(Decrease)
Compensation related costs	$ 9.7	$ 7.6	$ 2.1
Stock-based compensation	6.9	1.0	5.9
Legal and Professional Fees	2.6	6.0	(3.4)
Other general and administrative expenses	4.4	4.6	(0.2)
Total	$ 23.6	$ 19.2	$ 4.4

General and administrative expenses were $23.6 million and $19.2 million for the year ended December 31, 2021 and 2020, respectively.

General and administrative expenses increased by $4.4 million, compared to the same period in the prior year, primarily due to an increase of $8.0 million in compensation related costs, including stock-based compensation due to the initial recognition of modified stock option awards in September 2021 of $2.7 million, and an increase of $5.3 million as a result of increased hiring, partially offset by a decrease of $3.4 million in consulting and professional fees, as the prior year included professional fees related to the Redomiciliation Transaction.

Impairment of Intangible Assets

During the year ended December 31, 2020, we recognized an impairment charge of $0.9 million relating to our option over a non-financial intangible asset pursuant to an evaluation and option agreement with a collaboration partner. The partner was no longer conducting antibiotic candidate programs over which we had the option and thus, we assessed the fair value to be zero.

Other Operating Income

Other operating income was $21.0 million and $19.3 million for the year ended December 31, 2021 and 2020, respectively.

The increase in other operating income of $1.7 million for the year ended December 31, 2021, compared to the same period in the prior year is due to an increase of $5.8 million related to U.K. research and development tax credits for research and development expenses incurred that are not funded by third parties and an increase of $0.7 million in grant income received from CARB-X to progress the preclinical candidate, SMT-738, from the DDS-04 series for development in the fight against multi-drug resistant infections, offset by a decrease of $4.9 million in funding income from BARDA in support of our Ri-CoDIFy clinical trials and regulatory development of ridinilazole.

Other (Expense) Income, Net

Other expense, net was $2.4 million and other income, net was $0.3 million income for the year ended December 31, 2021 and 2020, respectively, and related primarily to changes in foreign exchange rates.

Income Tax Benefit

A tax benefit of $0.2 million was recognized for the year ended December 31, 2020 related to a tax refund recognized from the overpayment of estimated federal tax liabilities for previous tax years. The Company has recorded a full valuation allowance against the deferred tax assets in excess of our deferred tax liabilities, as the deferred tax liability represents future reversals of existing taxable temporary differences.

Liquidity and Capital Resources

Sources of Liquidity

To date, we have financed our operations primarily through issuances of our common stock (and before the Redomiciliation Transaction issuances of Summit Therapeutics plc's ordinary shares and American Depositary Shares, or ADSs), payments to us under license, collaboration, and commercialization arrangements, for example, our license and commercialization agreement with Eurofarma Laboratórios SA, or Eurofarma, and development funding and other assistance from government entities, philanthropic, non-government and not-for-profit organizations for our product candidates. In particular, we have received funding from BARDA, CARB-X, Innovate UK, Wellcome Trust and a number of not-for-profit organizations.

In January 2019, we received net proceeds of $24.4 million from the issuance and sale of 15,625,000 shares of common stock to a single investor, Mr. Robert W. Duggan. In December 2019, we received net proceeds of $49.1 million from the issuance and sale of 35,075,690 shares of common stock to three existing investors. As part of the equity placing, the participating investors were granted warrants with the right to subscribe for 5,261,353 new shares of common stock at an exercise price of $1.58 per share. On November 6, 2020, we received net proceeds of $50.0 million from the issuance and sale of 14,970,060 shares of common stock to three existing investors. Following the issuance of an unsecured promissory note on March 24, 2021, we received net proceeds of $55.0 million. Such note was later repaid without interest or penalty, rescinded and replaced by a new note on April 20, 2021, pursuant to a second unsecured promissory note we received net proceeds of $55.0 million. Subsequently, on May 12, 2021, we received proceeds of $75.0 million in the aggregate from the sale of 14,312,976 shares of Common Stock at a price per share of $5.24 from our rights offering, the proceeds of which were used in part to repay amounts outstanding on the second unsecured promissory note. On March 10, 2022, we received net proceeds of $25.0 million from the issuance of an unsecured promissory note (the "2022 Note") which becomes due upon the earlier of (i) the consummation of a registered public offering with net proceeds of no less than $25,000 or (ii) 18 months from the date of issuance of the 2022 Note.

We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed the development of any drugs. Since our inception, we have incurred significant operating losses. We anticipate that we will continue to incur losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, due to the nature and timing of our research and development activities. We expect that our research and development and general and administrative expenses will continue to be significant in connection with our ongoing research and development efforts. In addition, if we obtain marketing approval of ridinilazole in the United States or other jurisdictions where we retain commercial rights, and if we choose to retain those rights, we would expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses, as well as ongoing research and development expenses. In addition, our expenses will increase if and as we:

- continue the research and development of ridinilazole, as well as our early-stage programs targeting infections caused by Enterobacteriaceae;
- seek to identify and develop additional future product candidates, including through our bacterial genetics-based Discuva Platform for the discovery and development of new mechanism antibiotics, and specifically our research activities against a group of bacteria that collectively are known as the ESKAPE pathogens;
- seek marketing approvals for any product candidates that successfully complete clinical development;
- ultimately establish a sales, marketing and distribution infrastructure in jurisdictions where we have retained commercialization rights and scale up external manufacturing capabilities to commercialize any product candidates for which we receive marketing approval;
- acquire or in-license other product candidates and technology;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- expand our physical presence; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

During year ended December 31, 2021, we incurred a net loss of $88.6 million, and cash flows used in operating activities was $72.6 million. As of December 31, 2021 we had an accumulated deficit of $299.5 million, cash of $71.8 million, research and development tax credit receivable of $15.7 million and accounts receivable of $1.5 million. We expect to continue to generate operating losses for the foreseeable future. Based on our current funding arrangements and financial resources as of December 31, 2021 and after considering proceeds received of $25.0 million from the 2022 Note issued on March 10, 2022, the Company has the ability to fund its operating costs and working capital needs into the second half of 2023. Until we can generate substantial revenue and achieve profitability, we will need to raise additional capital to fund ongoing operations and capital needs. We will continue to review our data, including performing additional analyses on the microbiome and the relative impacts of ridinilazole and vancomycin in order to submit our data to the FDA. We have also determined, in light of our increased focus on the microbiome, that we may seek one or more third-party partnership opportunities for ridinilazole. In addition, we may consider and/or pursue business development opportunities to expand our pipeline of product candidates, including without limitation, potential acquisitions of and/or collaborations with other entities. While these capital resources will allow us to continue to evaluate our next steps, we will need additional capital to prepare for regulatory filings and commercial readiness, consider commencing additional trials, or consider other strategic alternatives with respect to ridinilazole or pursue other business development opportunities. Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition.

We have based the foregoing estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not obtain any additional funding through grants and clinical trial support or through new collaboration arrangements. Our future capital requirements will depend on many factors, including:

- the timing and evaluation of the data from our Phase III Ri-CoDIFy clinical trial for our lead product candidate, ridinilazole (formerly SMT19969), the next steps we will take with ridinilazole based upon our review, and the costs associated with these decisions, including completing our review of the data associated with Ri-CoDIFy and any partnerships into which we may enter to continue the advancement of ridinilazole;
- the number and development requirements of other future product candidates that we pursue;
- the costs, timing and outcome of regulatory review of ridinilazole and our other product candidates we develop;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- subject to receipt of marketing approval, revenue received from commercial sales of ridinilazole or any other product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims;
- our contract with BARDA and whether BARDA elects to pursue its final designated option beyond the base period and two exercised options;
- the amounts we receive from Eurofarma under our license and commercialization agreement, including for the achievement of development, commercialization and sales milestones and for product supply transfers;
- our ability to establish and maintain third-party partnerships or other arrangements and the financial terms of such arrangements;
- the extent to which we acquire or invest in other businesses, products and technologies;
- the rate of the expansion of our physical presence;
- the extent to which we change our physical presence

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of some, or all, of the following: equity and debt offerings, collaborations, strategic alliances, grants and clinical trial support from government entities, philanthropic, non-government and not-for-profit organizations and, marketing, distribution or licensing arrangements. We do not have any committed external source of funds other than amounts we may receive from Eurofarma, BARDA, CARB-X and under our arrangements with them and our research and development tax credits receivable.

We will be entitled to receive an additional $1.5 million from Eurofarma for the achievement of various development milestones and we are eligible to receive up to $21.4 million in development, commercial and sales milestones when cumulative net sales equal or exceed $100.0 million in the Eurofarma licensed territory. Each subsequent achievement of an additional $100.0 million in cumulative net sales will result in the Company receiving additional milestone payments, which, when combined with anticipated product supply transfer payments from Eurofarma paid to the Company in connection with a commercial supply agreement to be entered into between the two parties, will provide payments estimated to range from a mid-

teens to high-teens percentage of cumulative net sales in the territories where we have granted Eurofarma commercialization rights. As of December 31, 2021, we have recognized $3.9 million of cumulative income since inception.

The total amount of committed BARDA funding is $62.4 million. As of December 31, 2021, an aggregate of $56.5 million of the total committed BARDA funding has been received and we have recognized $50.3 million of cumulative income since contract inception. The total amount of committed CARB-X funding is $4.1 million, with the possibility of up to another $3.7 million based on the achievement of future milestones. As of December 31, 2021, an aggregate of $0.5 million of grant funding from CARB-X has been received and we have recognized $1.2 million of cumulative income since inception.

We will need additional capital to fund our operations. Additional capital, when needed, may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we will be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

The following table summarizes the results of our cash flows for the years ended December 31, 2021 and 2020.

	Year Ended December 31, 2021	Year Ended December 31, 2020
Net cash used in operating activities	(72,587)	(48,111)
Net cash used in investing activities	(306)	(421)
Net cash provided by financing activities	77,916	50,551

Operating Activities

Net cash used in operating activities for the year ended December 31, 2021 was $72.6 million and resulted from a net loss of $88.6 million, which included non-cash charges of $16.1 million, which is primarily comprised of $12.8 million of stock-based compensation, and a $0.1 million net increase in working capital. The net increase in working capital was primarily due to an a $6.0 million increase in the research and development tax credit receivable, a $1.7 million decrease in accounts payable, a $1.1 million increase in accounts receivable, a $1.1 million decrease in lease liabilities and a $0.8 million decrease in deferred revenue partially offset by a $8.2 million increase in accrued liabilities and accrued compensation and a $2.3 million decrease in prepaid expenses.

Net cash used in operating activities for the year ended December 31, 2020 was $48.1 million and resulted from a net loss of $52.7 million, which included non-cash charges of $4.0 million, which is primarily comprised of $1.8 million in stock-based compensation and $1.2 million in amortization of intangible assets, and a net decrease in working capital of $0.6 million. The net decrease in working capital was primarily due to a $5.4 million increase in deferred revenue and other income and an increase of $1.6 million in accounts payable, partially offset by an increase in the research and development tax credit receivable of $4.4 million, a decrease of $1.3 million in accrued liabilities and accrued compensation, a $0.5 million decrease in lease liabilities.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 of $0.3 million was for the purchase of property and equipment.

Net cash outflow in investing activities for the year ended December 31, 2020 was $0.4 million was for the purchase of property and equipment.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $77.9 million and primarily resulted from net proceeds of $74.8 million from the rights offering in May 2021, proceeds from the promissory notes from a related party of $110.0 million, offset by repayments of the promissory notes from a related party of $110.0 million and $3.1 million of net proceeds from the exercise of stock options.

Net cash provided by financing activities for the year ended December 31, 2020, was $50.6 million and resulted from net proceeds of $50.0 million received from a private placement of common stock in November 2020, and $0.6 million of net proceeds from the exercise of stock options.

Contractual Obligations and Commitments

The following table summarizes our lease contractual obligations as of December 31, 2021.

	Payment due by period				
(in millions)	**Total**	**Less than 1 year**	**Between 1 and 3 years**	**Between 3 and 5 years**	**More than 5 years**
Operating lease obligations	$2.9	$1.0	$1.5	$0.4	$—

The preceding table excludes contingent payment obligations which primarily consist of commitments under our agreements with the Wellcome Trust, the University College London and certain employees, former employees and former directors of Discuva, pursuant to which we will be required to pay royalties or make milestone payments.

As of December 31, 2021, we were unable to estimate the amount, timing or likelihood of achieving the milestones or making future product sales that these contingent payment obligations relate to. For additional information regarding these agreements, see “Business—Our Collaborations and Funding Arrangements” in this Annual Report on Form 10-K.

Additionally, we enter into contracts in the normal course of business with various third parties for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. Most contracts provide for termination upon notice, and therefore are cancellable contracts. As of December 31, 2021, total contractual commitments are estimated to be approximately $17.0 million and the majority of these commitments are due within one year.

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, intangible assets, accrued research and development expenses, stock-based compensation and income taxes. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe the following critical accounting policies affect the most significant judgments, assumptions and estimates we use in preparing the consolidated financial statements:

Revenue Recognition

The Company accounts for revenue using Accounting Standards Codification ("ASC") 606 ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards.

The Company enters into out-licensing agreements within the scope of ASC 606 under which it licenses certain rights to its product candidates to third parties. Such agreements may include the transfer of intellectual property rights in the form of

licenses, transfer of technological know-how, delivery of drug substances, research and development services, and participation on certain committees with the counterparty. Payments made by the customers may include one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services the Company provides through its contract manufacturers; and royalties on net sales of licensed products if they are successfully approved and commercialized. Each of these payments may result in license, collaboration, or other revenue, except revenue from royalties on net sales of licensed products, which would be classified as royalty revenue.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its out-licensing agreements, the following steps are performed: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. Revenue is then recognized in respect of the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. As part of the accounting for these arrangements, the Company must use significant judgment to determine: (a) the performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; and (c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company also uses judgment to determine whether milestone payments or other variable consideration, except for royalties and sales-based milestones, should be included in the transaction price, as described below. The transaction price is allocated to each performance obligation based on the relative standalone selling price of each performance obligation in the contract, and the Company recognizes revenue based on those amounts when, or as, the performance obligations under the contract are satisfied.

Exclusive Licenses

If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from nonrefundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition. The measure of progress, and the resulting periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research, development and licensing arrangement. Such a change could have a material impact on the amount of revenue the Company records in future periods. Under the Company's existing license and collaboration agreements, the Company has concluded that the transfer of control to the customer occurs over the time period that the research and development services are to be provided by the Company, and this output method is, in management's judgment, the best measure of progress towards satisfying the performance obligation.

Milestone Payments

At the inception of each arrangement that includes potential research, development or regulatory milestone payments, the Company evaluates whether the milestones are considered likely to be met and estimates the amount to be considered for inclusion in the transaction price using the most-likely-amount method. If it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur, the associated milestone payment value is included in the transaction price. For milestone payments due upon events that are not within the control of the Company or the licensee, such as regulatory approvals, the Company is not able to assert that it is likely that the regulatory approval will be granted and that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur until those approvals are received. In making this assessment, the Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone. There is considerable judgment involved in determining whether it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur. At the end of each

subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price of the arrangement. Any such adjustments are recorded on a cumulative catch-up basis, which would affect the amounts of revenue and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments due upon first commercial sales or based on a level of sales, that are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) the occurrence of the related sales or (ii) the date upon which the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. To date, the Company has not recognized any royalty revenue from any of its licensing arrangements.

Intangible Assets

Intangible assets include patents, licenses, an option over non-financial assets and a research and development discovery platform ("Discuva Platform").

Patents, licenses, and the option over non-financial assets are initially recorded at fair value, assigned an estimated useful life, and amortized primarily on a straight-line basis over their estimated useful lives. The Company evaluates the recoverability of its intangible and long-lived assets whenever events and changes in circumstances indicate that the carrying amount of an asset may not be fully recoverable. If events and circumstances indicate that the carrying amount may not fully be recoverable, the Company will perform a qualitative assessment, and consider certain events and circumstances specific to the intangible asset and to the entity as a whole, such as macroeconomic conditions, industry and market considerations, overall financial performance and cost factors when evaluating whether it is more likely than not that the fair value of the intangible asset is less than its carrying amount. This periodic review may result in an adjustment of estimated depreciable lives or asset impairment. When indicators of impairment are present, the carrying values of the asset are evaluated in relation to their operating performance and future undiscounted cash flows of the underlying business. If the future undiscounted cash flows are less than their carrying value, impairment exists. The impairment is measured as the difference between the carrying value and the fair value of the underlying asset. Fair values are based on estimates of market prices and assumptions concerning the amount and timing of estimated future cash flows and assumed discount rates, reflecting varying degrees of perceived risk.

Other intangible assets are amortized in equal installments over their estimated useful lives as follows:

Intangible Asset	Amortization Period
Option over non-financial assets	Over the period of the relevant agreement

Amortization of intangible assets is included as part of the research and development expense line shown on the face of the consolidated statement of operations and comprehensive loss.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred to discover, research and develop product candidates, including personnel expenses, stock-based compensation expense, allocated facility-related and depreciation expenses, third-party license fees and external costs of outside vendors engaged to conduct preclinical and clinical development activities and clinical trials as well as to manufacture clinical trial materials. Non - refundable prepayments for goods or services that will be used or rendered for future research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced. Milestone and other payments made to third-parties with respect to in-process research and development, in accordance with the Company’s license, acquisition and other similar agreements are expensed when determined to be probable and estimable.

The Company has entered into various research and development contracts with other companies. These agreements are generally cancellable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs or prepaid expenses where the payments made exceeds the estimated costs. When evaluating the adequacy of these balances, the Company analyzes progress of the studies, including the estimated costs to complete each study or activity, the estimation of the current stage of completion and the invoices received, as well as predetermined milestones which are not reflective of the current stage of development for prepaid expenses. Actual results could differ from the Company’s estimates. In all cases, the full cost of each study or activity is expensed by the

time the final report or where applicable, product, has been received. The Company's historical estimates have not been materially different from the actual costs.

Stock-Based Compensation

The Company measures and recognizes compensation expense for all stock option and restricted stock unit awards based on the estimated fair value of the award on the grant date. The Company uses the Black-Scholes option pricing model to estimate the fair value of stock option awards. The fair value is recognized as expense, over the requisite service period, which is generally the vesting period of the respective award, on a straight-line basis for each separately vesting portion of the award when the only condition to vesting is continued service. If vesting is subject to a market or performance condition, recognition is based on the derived service period of the award. Expense for awards with performance conditions is estimated and adjusted on a quarterly basis based upon the assessment of the probability that the performance condition will be met. Use of the Black-Scholes option-pricing model requires management to apply judgment under highly subjective assumptions. These assumptions include:

- Expected term—The expected term of stock options represents the weighted-average period the stock options are expected to be outstanding. The Company uses the simplified method for estimating the expected term as provided by the Securities and Exchange Commission. The simplified method calculates the expected term as the average of the time-to-vesting and the contractual life of the options.
- Expected volatility—The expected volatility was calculated based on historical volatility of the Company's share price.
- Risk-free interest rate—The risk-free rate assumption is based on the U.S. Treasury instruments, the terms of which were consistent with the expected term of the Company's stock options.
- Expected dividend—The expected dividend assumption is based on the Company's history and expectation of dividend payouts. The Company has not paid and does not intend to pay dividends.

The Company estimates expected forfeitures at the time of grant instead of accounting for forfeitures as they occur. Stock option and restricted stock unit awards have been granted at fair value to non-employees, in connection with research and consulting services provided to the Company, to non-employees in connection with corporate activities, and to employees, in connection with Stock Purchase and Restriction Agreements. Equity awards generally vest over terms of 3 or 4 years.

Income Taxes

The provision for income taxes is determined using the asset and liability approach. Tax laws may require items to be included in tax filings at different times than the items are reflected in the financial statements. A current asset or liability is recognized for the estimated taxes receivable or payable for the current year. Deferred taxes represent the future tax consequences expected to occur when the reported amounts of assets and liabilities are recovered or paid. Deferred taxes are initially recognized at enacted tax rates in force at the time of initial recognition and are subsequently adjusted for any enacted changes in tax rates and tax laws. Subsequent changes to deferred taxes originally recognized in equity are recognized in income. Valuation allowances are recorded to reduce deferred tax assets when it is more likely than not that a tax benefit will not be realized. The Company has recorded a full valuation allowance against the deferred tax assets in excess of its deferred tax liabilities, as the deferred tax liability represents future reversals of existing taxable temporary differences. The Company records interest and penalties related to income tax matters as part of income tax expense.

Recent Accounting Pronouncements

For a discussion of recent accounting pronouncements, please see Note 5 to our consolidated financial statements contained in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our primary exposures to market risk are liquidity risk and foreign currency risk.

Liquidity Risk

We have funded our operations since inception primarily through the issuance of equity and debt securities. We have also received funding from our license, collaboration, and commercialization arrangements, for example, our license and commercialization agreement with Eurofarma, as well as philanthropic, non-government and not-for-profit organizations and grant funding from government entities, including BARDA, CARB-X, Innovate UK, Wellcome Trust and a number of not-for-profit organizations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Foreign Currency Risk

Foreign currency risk refers to the risk that the value of a financial commitment or recognized asset or liability will fluctuate due to changes in foreign currency rates. Our net loss and financial position, as expressed in U.S. dollar, are exposed to movements in foreign exchange rates against the pounds sterling and the euro. The main trading currencies are pounds sterling, the U.S. dollar, and the euro. We are exposed to foreign currency risk as a result of operating transactions and the translation of foreign bank accounts. We monitor our exposure to foreign exchange risk. Exposures are generally managed through natural hedging via the currency denomination of cash balances and any impact currently is not material to us.

Interest Rate Risk

We do not hold any derivative instruments, or other financial instruments, that expose us to material interest rate risk.

Credit Risk

We consider all of our material counterparties to be creditworthy. We consider the credit risk for each of our counterparties to be low and do not have a significant concentration of credit risk at any of our counterparties. We had $1.5 million of accounts receivable outstanding at December 31, 2021, due primarily from BARDA. This amount was collected subsequent to the period end. We also have a $15.7 million of research and development tax credits outstanding at December 31, 2021. Given that these receivables related to U.K. research and development tax credit cash rebate regimes and given our history of collection, it is highly unlikely that these amounts will not be collected.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are included to this Report. An index of those financial statements is found in Item 15.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We have carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) under the supervision and the participation of the company's management, which is responsible for the management of the internal controls, and which includes our Chief Executive Officer (our Principal Executive Officer and Principal Financial Officer). The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act of 1934 is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives. Based upon our evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer (our Principal Executive Officer and Principal Financial Officer) concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable level of assurance.

Management's Report on Internal Control Over Financial Reporting and Attestation Report of Registered Public Accounting Firm

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed, under the supervision of the Chief Executive Officer (our Principal Executive Officer and Principal Financial Officer), to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with Generally Accepted Accounting Principles.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect all misstatements. Moreover, projections of any evaluation of the effectiveness of internal control to future periods are subject to a risk that controls may become inadequate because of changes in conditions and that the degree of compliance with the policies or procedures may deteriorate.

Our management has assessed the effectiveness of internal control over financial reporting as of December 31, 2021, based on the Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) 2013. Based on this assessment, our management has concluded that our internal control over financial reporting as of December 31, 2021, was effective.

This report does not include an attestation report of our registered public accounting firm as we are a non-accelerated filer and a smaller reporting company.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

The Compensation Committee of the Company's Board of Directors reviewed and approved employee 2021 bonuses. A discretionary cash bonus of $182,250 is scheduled to be paid to Maky Zanganeh, the Company's Chief Operations Officer, on March 25, 2022.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 11. Executive Compensation

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(1) **Financial Statements**

As part of this Report, the consolidated financial statements are listed in the accompanying index to financial statements on page 91.

(2) **Financial Statement Schedules**

All financial statement schedules have been omitted because they are not applicable, not required, or the information required is shown in the consolidated financial statements or the notes thereto.

(3) **Exhibits**

The exhibits filed as part of this Report are listed below.

Exhibit No.	Description
2.1	Scheme of Arrangement, dated September 18, 2020 (incorporated by reference to Exhibit 99.1 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on July 27, 2020)
3.1	Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
4.1	Registration Rights Agreement, dated January 9, 2019, by and among Summit Therapeutics plc and Robert W. Duggan (incorporated by reference to Exhibit 2.1 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on January 10, 2019)
4.2	Form of Specimen Stock Certificate (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 29, 2020)
4.3	Form of Consultant Warrant (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
4.4	Form of Investor Warrant (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
4.5	Description of Securities Registered Under Section 12 of the Exchange Act (incorporated by reference to the description of securities contained in the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
4.6	Registration Rights Agreement, dated November 6, 2020, by and among Summit Therapeutics Inc., Polar Capital Funds plc - Biotechnology Fund and the Mahkam Zanganeh Revocable Trust (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on November 6, 2020)
4.7	Form of Subscription Rights Certificate (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on April 21, 2021)
10.1†	Translation Award Funding Agreement, entered into as of October 19, 2012, by and between the Wellcome Trust Limited and Summit Therapeutics plc (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 27, 2015)
10.2	Service Agreement, effective as of January 14, 2015, by and between Cambridge Innovation Center and Summit Therapeutics Inc. (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
10.3#	2005 Enterprise Management Incentive Scheme (incorporated by reference to Exhibit 4.3 to the Company's Transition Report on 20-F (File No. 333-36866), as amended, filed with the Securities and Exchange Commission on April 30, 2020)
10.4#	2016 Long Term Incentive Plan (incorporated by reference to Exhibit 4.22 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on May 12, 2016)
10.5†	License and Collaboration Agreement, dated October 3, 2016, by and between Summit (Oxford) Ltd. and Sarepta Therapeutics, Inc. (incorporated by reference to Exhibit 4.23 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on March 30, 2017)

Exhibit No.	Description
10.6	Lease, dated February 17, 2017, by and among MEPC Milton Park No. 1 Limited, MEPC Milton Park No. 2 Limited and Summit Therapeutics plc (incorporated by reference to Exhibit 4.25 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on March 30, 2017)
10.7†	Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.26 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.8†	Amendment of Solicitation/Modification of Contract (0001), dated June 19, 2018, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.13 to the Company's Transition Report on 20-F (File No. 333-36866) filed with the Securities and Exchange Commission on March 29, 2019)
10.9+	Amendment of Solicitation/Modification of Contract (0002), dated August 14, 2018, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.14 to the Company's Transition Report on 20-F(File No. 333-36866) filed with the Securities and Exchange Commission on March 29, 2019)
10.10+	Amendment of Solicitation/Modification of Contract (0003), dated February 14, 2019, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.15 to the Company's Transition Report on 20-F (File No. 333-36866), filed with the Securities and Exchange Commission on March 29, 2019)
10.11†	License and Commercialization Agreement, dated December 18, 2017, by and between Summit (Oxford) Ltd. and Eurofarma Laboratórios S.A. (incorporated by reference to Exhibit 4.27 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.12†[(1)]	Share Purchase Agreement, dated December 23, 2017, by and among Summit Therapeutics plc and the shareholders of Discuva Limited (incorporated by reference to Exhibit 4.28 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.13†	Transfer Incentive Agreement, dated December 23, 2017, by and among Discuva Limited and certain of its managers (incorporated by reference to Exhibit 4.29 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.14	Lease, dated December 22, 2017, by and between Merrifield Centre Ltd and Discuva Limited (incorporated by reference to Exhibit 4.31 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.15†	Equity and Revenue Sharing Agreement, dated October 16, 2017, by and between Summit (Oxford) Limited and the Wellcome Trust Limited (incorporated by reference to Exhibit 4.32 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.16	Form of Non-Executive Director Restricted Stock Unit (RSU) Agreement (incorporated by reference to Exhibit 4.33 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
10.17	Securities Purchase Agreement, dated December 14, 2018, by and among Summit Therapeutics plc and Robert W. Duggan (incorporated by reference to Exhibit 10.1 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 17, 2018)
10.18+	Amendment of Solicitation/Modification of Contract (0004), dated June 17, 2019, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.24 to the Company's Transition Report on 20-f (File No. 333-36866) filed with the Securities and Exchange Commission on April 30, 2020)

Exhibit No.	Description
10.19	Securities Purchase Agreement, dated December 6, 2019, by and among Summit Therapeutics plc and Robert W. Duggan (incorporated by reference to Exhibit 4.1 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 6, 2019)
10.20	Placing Agreement, December 6, 2019, by and between Summit Therapeutics plc and Nplus1 Singer Advisory LLP (incorporated by reference to Exhibit 4.2 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 6, 2019)
10.21	Consulting Agreement, dated December 6, 2019, by and between Summit Therapeutics plc and Maky Zanganeh & Associates, Inc. (incorporated by reference to Exhibit 4.4 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 6, 2019)
10.22	Relationship Agreement, dated December 14, 2018, by and among Summit Therapeutics plc, Robert W. Duggan and Cairn Financial Advisers LLP (incorporated by reference to Exhibit 10.2 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 17, 2018)
10.23	Deed of Termination, dated December 6, 2019, by and among Summit Therapeutics plc, Robert Duggan and Cairn Financial Advisers LLP (incorporated by reference to Exhibit 4.3 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 6, 2019)
10.24+	Amendment of Solicitation/Modification of Contract (0005), dated January 21, 2020, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.36 to the Company's Transition Report on 20-F (File No. 333-36866) filed with the Securities and Exchange Commission on April 30, 2020)
10.25[(1)]	Securities Purchase Agreement, dated October 2, 2020, by and between Summit Therapeutics Inc. and Robert W. Duggan (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-36866) filed with the Securities and Exchange Commission on October 5, 2020)
10.26[(1)]	Securities Purchase Agreement, dated November 6, 2020, by and between Summit Therapeutics Inc. and Polar Capital Fund plc - Biotechnology Fund (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-36866) filed with the Securities and Exchange Commission on November 6, 2020)
10.27[(1)]	Securities Purchase Agreement, dated November 6, 2020, by and between Summit Therapeutics Inc. and Mahkam Zanganeh Revocable Trust (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-36866) filed with the Securities and Exchange Commission on November 6, 2020)
10.28#	Form of Indemnification Agreement between Summit Therapeutics Inc. and each of its Executive Officers and Directors (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
10.29#	Offer of Employment, dated May 21, 2020, by and between Summit Therapeutics Inc. and Michael Donaldson (incorporated by reference to Exhibit 10.25 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 29, 2020)
10.30#	Contract of Employment, dated May 29, 2020, by and between Summit Therapeutics Inc. and Ventzislav Stefanov (incorporated by reference to Exhibit 10.26 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 29, 2020)
10.31#	2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
10.32#	Form of Option Award under 2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.28 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 29, 2020)
10.33#	Form of Restricted Stock Unit Agreement under 2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.29 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 29, 2020)
10.34#	2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)

Exhibit No.	Description
10.35	Contract of Employment, dated November 22, 2020, by and between Summit Therapeutics Inc. and Mahkam Zanganeh (incorporated by reference to Exhibit 10.35 to the Company's Annual Report on Form 10-K (File No. 001-36866), filed with the Securities and Exchange Commission on March 31, 2021)
10.36	Sublease Agreement, dated March 26, 2021, by and between Maky Zanganeh & Associates Inc. and Summit Therapeutics Sub Inc. (incorporated by reference to Exhibit 10.36 to the Company's Annual Report on Form 10-K (File No. 001-36866), filed with the Securities and Exchange Commission on March 31, 2021)
10.37	Exit Agreement, dated May 28, 2021, by and between Summit Therapeutics Inc. and Michael Donaldson (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on May 28, 2021)
10.38(1)	Note Purchase Agreement, dated March 10, 2022, by and between Summit Therapeutics Inc. and Robert W. Duggan (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File. No. 001-36866), filed with the Securities and Exchange Commission on March 11, 2022)
10.39	Promissory Note, dated March 10, 2022, in the name of Robert W. Duggan (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File. No. 001-36866), filed with the Securities and Exchange Commission on March 11, 2022)
16.1	Letter from PwC to the Securities and Exchange Commission, dated May 26, 2021 (incorporated by reference to Exhibit 16.1 to the Company's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on May 26, 2021)
21.1*	List of Significant Subsidiaries
23.1*	Consent of PricewaterhouseCoopers LLP, a Delaware limited liability partnership
23.2*	Consent of PricewaterhouseCoopers LLP, a United Kingdom entity
31.1*	Certification of Chief Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002
32.1*	Certification pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

*	Filed herewith.
†	Confidential treatment has been granted as to certain portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.
+	Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the registrant if disclosed.
(1)	The schedules and exhibits have been omitted. A copy of any omitted schedule or exhibit will be furnished to the Securities and Exchange Commission upon request.
#	Indicates management contract or compensatory plan or arrangement.

Item 16. Report Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

SUMMIT THERAPEUTICS INC.

By:	/s/ Robert W. Duggan
Name:	Robert W. Duggan
Title:	Chief Executive Officer and Executive Chairman; Principal Executive Officer and Principal Financial Officer

Date: March 17, 2022

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Robert W. Duggan Robert W. Duggan	Chief Executive Officer and Executive Chairman; Principal Executive Officer and Principal Financial Officer	March 17, 2022
/s/ Mahkam Zanganeh Mahkam Zanganeh	Chief Operations Officer and Director	March 17, 2022
/s/ Kenneth Clark Kenneth Clark	Director	March 17, 2022
/s/ Urte Gayko Urte Gayko	Director	March 17, 2022
/s/ Ujwala Mahatme Ujwala Mahatme	Director	March 17, 2022
/s/ Manmeet Soni Manmeet Soni	Director	March 17, 2022

Summit Therapeutics Inc.

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Index to the Financial Statements

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Summit Therapeutics Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Summit Therapeutics Inc. and its subsidiaries (the "Company") as of December 31, 2021, and the related consolidated statements of operations and comprehensive loss, of stockholders' equity and of cash flows for the year then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and the results of its operations and its cash flows for the year then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audit provides a reasonable basis for our opinion.

Emphasis of Matter

As discussed in Note 3 to the consolidated financial statements, the Company will require additional financing to fund its ongoing operations. Management's evaluation of the events and conditions and management's plans to mitigate this matter is also described in Note 3.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued and Prepaid Research and Development Costs

As described in Notes 4 and 14 to the consolidated financial statements, included within prepaid expenses as of December 31, 2021 is $6.1 million of prepayments relating to research and development expenditures. Included within accrued liabilities as of December 31, 2021 is $5.2 million relating to research and development expenditures. The Company records accruals for estimated ongoing research and development costs or prepaid expenses where the payments made exceed the estimated costs. These amounts are determined by management based on the estimated costs to complete each study or activity, the estimation of the current stage of completion and the invoices received, as well as predetermined milestones which are not reflective of the current stage of development for prepaid expenses. However, prepaid expenses decrease, and accrued liabilities increase as the activities progress, and if actual costs incurred exceed the prepaid expense, an accrual will be recorded for the liability. The key sensitivity is the estimated current stage of completion of each study or activity, which is based on information received from the supplier and management's operational knowledge of the work completed under those contracts.

The principal considerations for our determination that performing procedures relating to accrued and prepaid research and development costs is a critical audit matter are the significant judgment by management when determining the estimated research and development costs, which in turn led to significant auditor judgment, subjectivity, and effort in performing procedures and evaluating audit evidence related to estimated current stage of completion of each study or activity.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others, (i) evaluating management's process on a sample basis for determining the current stage of completion of each study or activity; (ii) reading a sample of research and development contracts; (iii) evaluating the reasonableness of progress towards completion for a sample of research and development activities and the associated incurred cost based on invoices, external confirmations or other information received from the supplier; and (iv) testing the completeness and accuracy of the underlying data including total costs included within contracts and actual billed amounts for a sample of contracts.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 17, 2022

We have served as the Company's auditor since 2021.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Summit Therapeutics Inc.

Opinion on Financial Statements

We have audited the consolidated balance sheet of Summit Therapeutics Inc. and its subsidiaries (the "Company") as of December 31, 2020, and the related Consolidated Statements of Operations and Comprehensive Loss, of Stockholders' Equity and of Cash Flows for the year ended December 31, 2020 including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020, and the results of its operations and its cash flows for the year ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Reading, United Kingdom
March 17, 2022

We served as the Company's auditor from 2013 to 2020.

Summit Therapeutics Inc.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash	$ 71,791	$ 66,417
Accounts receivable	1,464	331
Prepaid expenses	7,161	9,547
Other current assets	1,201	1,523
Research and development tax credit receivable	15,695	9,856
Total current assets	97,312	87,674
Non-current assets:		
Property and equipment, net	694	725
Right-of-use assets	2,790	554
Goodwill	2,009	2,030
Intangible assets, net	10,399	11,515
Other assets	170	—
Total assets	$ 113,374	$ 102,498
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,374	$ 6,140
Accrued liabilities	7,197	3,278
Accrued compensation	4,125	983
Lease liabilities	1,091	390
Deferred revenue and other income	7,939	8,370
Other current liabilities	897	729
Total current liabilities	25,623	19,890
Non-current liabilities		
Lease liabilities, net of current portion	1,691	75
Deferred revenue and other income, net of current portion	—	569
Other non-current liabilities	2,776	2,511
Total liabilities	30,090	23,045
Commitments and contingencies (Note 19)		
Stockholders' equity:		
Common stock, $0.01 par value: 250,000,000 shares authorized; 98,039,540 and 82,575,064 shares issued and outstanding at December 31, 2021 and 2020, respectively	980	826
Additional paid-in capital	384,049	293,367
Accumulated other comprehensive loss	(2,197)	(3,794)
Accumulated deficit	(299,548)	(210,946)
Total stockholders' equity	83,284	79,453
Total liabilities and stockholders' equity	$ 113,374	$ 102,498

The accompanying notes are an integral part of the consolidated financial statements

Summit Therapeutics Inc.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31, 2021	Year Ended December 31, 2020
Revenue	$ 1,809	$ 860
Operating expenses:		
Research and development	85,352	53,274
General and administrative	23,611	19,232
Impairment of intangible assets	—	859
Total operating expenses	108,963	73,365
Other operating income	20,968	19,312
Operating loss	(86,186)	(53,193)
Other (expense) income, net	(2,416)	283
Loss before income tax	(88,602)	(52,910)
Income tax benefit	—	213
Net loss	$ (88,602)	$ (52,697)
Net loss per share:		
Basic and diluted	$ (0.96)	$ (0.76)
Weighted average common shares outstanding:		
Basic and diluted	92,239,306	69,524,148
Other comprehensive (loss) income:		
Foreign currency translation adjustments	1,597	970
Comprehensive loss	$ (87,005)	$ (51,727)

The accompanying notes are an integral part of the consolidated financial statements.

Summit Therapeutics Inc.
Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Total Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	67,178,054	$ 672	$ 241,204	$ (4,764)	$ (158,249)	$ 78,863
Private placement of common stock, net of offering costs of $48	14,970,060	150	49,802	—	—	49,952
Fractional shares issued from reverse stock split	3	—	—	—	—	—
Issuance on common stock from exercise of share options	426,947	4	595	—	—	599
Stock-based compensation	—	—	1,766	—	—	1,766
Foreign currency translation adjustment	—	—	—	970	—	970
Net loss	—	—	—	—	(52,697)	(52,697)
Balance at December 31, 2020	82,575,064	$ 826	$ 293,367	$ (3,794)	$ (210,946)	$ 79,453
Rights offering of common stock, net of offering costs of $159	14,312,976	143	74,698	—	—	74,841
Issuance of common stock from exercise of stock options	1,151,500	11	3,077	—	—	3,088
Stock-based compensation	—	—	12,804	—	—	12,804
Imputed interest expense on promissory note payable to a related party	—	—	103	—	—	103
Foreign currency translation adjustment	—	—	—	1,597	—	1,597
Net loss	—	—	—	—	(88,602)	(88,602)
Balance at December 31, 2021	98,039,540	$ 980	$ 384,049	$ (2,197)	$ (299,548)	$ 83,284

The accompanying notes are an integral part of the consolidated financial statements.

Summit Therapeutics Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31, 2021	Year Ended December 31, 2020
Cash flows used in operating activities:		
Net loss	$ (88,602)	$ (52,697)
Adjustments to reconcile net loss to net cash used in operating activities:		
Gain on remeasurement of liabilities	—	(480)
Gain on recognition of contingent consideration payable	—	(102)
Non-cash interest expense	196	255
Unrealized foreign exchange loss (gain)	326	(278)
Amortization of operating right-of-use assets	1,108	451
Depreciation	330	302
Amortization of intangible assets	1,017	1,250
Impairment of intangible assets	—	859
Stock-based compensation	12,804	1,766
Other adjustments	301	(56)
Changes in operating assets and liabilities:		
Accounts receivable	(1,138)	212
Prepaid expenses	2,345	(447)
Other current and long-term assets	104	(24)
Research and development tax credit receivable	(6,015)	(4,381)
Deferred revenue and other income	(813)	5,372
Accounts payable	(1,711)	1,642
Accrued liabilities and accrued compensation	8,229	(1,296)
Operating lease liabilities	(1,068)	(459)
Net cash used in operating activities	(72,587)	(48,111)
Cash flows used in investing activities:		
Purchase of property and equipment	(306)	(421)
Net cash used in investing activities	(306)	(421)
Cash flows provided by financing activities:		
Proceeds from the issuance of common stock	75,000	50,000
Transaction costs from the issuance of common stock	(118)	(48)
Proceeds from related party promissory notes	110,000	—
Re-payment of related party promissory notes	(110,000)	—
Payments of related party promissory notes issuance costs	(54)	—
Proceeds from exercise of share options	3,088	599
Net cash provided by financing activities	77,916	50,551
Effect of exchange rates on cash	351	556
Increase in cash	5,374	2,575
Cash at beginning of period	66,417	63,842
Cash at end of period	$ 71,791	$ 66,417
Supplemental Disclosure of Cash Flow Information		
Cash paid for interest on related party promissory note	$ 85	$ —
Cash paid (received) for income taxes	$ 7	$ (70)
Transaction costs included in accrued expenses	$ 41	$ —
Leased assets obtained in exchange for operating lease liabilities	$ 3,389	$ —

The accompanying notes are an integral part of the consolidated financial statements.

Notes to Consolidated Financial Statements

1. Nature of Business and Operations and Recent Events

Nature of Business and Operations

The Company is a biopharmaceutical company focused on the discovery, development, and commercialization of patient-, physician-, caregiver- and societal-friendly medicinal therapies intended to improve quality of life, increase life expectancy, and resolve serious unmet needs. The Company's novel mechanism pipeline of product candidates is designed with the goal to become the patient-friendly, new-era standard-of-care medicines, and to work in harmony with the human microbiome. Currently, the Company's lead product candidate, ridinilazole, is a novel first-in-class drug that is engaged in a global Phase III clinical trial program. On December 20, 2021, the Company announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole for treating patients suffering from *Clostridioides difficile* infection, also known as *C. difficile* infection, or CDI. The Company's second product candidate, SMT-738, was announced in May 2021 for combating multidrug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae (“CRE”) infections. SMT-738 is the first of a novel class of precision antibiotics that has entered into preclinical development. The Company intends to expand its portfolio by developing further new mechanism, new era product offerings that are designed to work in harmony with the human gut microbiome in the therapeutic areas of oncology and infectious diseases.

On September 18, 2020, Summit Therapeutics Inc. ("Summit"), a Delaware corporation, became the successor issuer to Summit Therapeutics plc, a public limited company incorporated under the laws of England and Wales with the Registrar of Companies of England and Wales, United Kingdom ("U.K."), for certain purposes under both the Securities Act of 1933, as amended, and the Securities Exchange Act of 1934, as amended, or the Exchange Act. Such succession occurred pursuant to a statutory scheme of arrangement under U.K. law pursuant to which all Summit Therapeutics plc outstanding ordinary shares were exchanged on a five-for-one basis for newly issued shares of Summit common stock and Summit became the holding company of Summit Therapeutics plc (the predecessor registrant and former holding company) and its subsidiaries (which is referred to as the "Redomiciliation Transaction"). Concurrently, Summit Therapeutics plc was converted into a private limited company under the laws of England and Wales and renamed Summit Therapeutics Limited. In addition, the warrants and stock options to purchase shares of Summit Therapeutics plc were canceled and replacement warrants and stock options to purchase common stock in Summit Therapeutics Inc. were issued. The scheme of arrangement was accounted for as an exchange of equity interests among entities under common control. All assets and liabilities of Summit Therapeutics plc were assumed by Summit, resulting in the retention of the historical basis of accounting as if they had always been combined for accounting purposes and the historical consolidated financial statements of Summit Therapeutics plc became the historical consolidated financial statements of Summit Therapeutics Inc. All share and per share data for periods prior to the Redomiciliation Transaction in the financial statements were retroactively reflected to be presented as shares of the Company's common stock, par value $0.01 per share.

Recent Events

On May 12, 2021, the Company closed its rights offering, which was fully subscribed. The Company received aggregate gross proceeds from the rights offering of $75,000 from the sale of 14,312,976 shares of its common stock at a price per share of $5.24. Issuance costs associated with the rights offering were immaterial. In connection with the closing of the rights offering, a promissory note, dated April 20, 2021, was issued by the Company in favor of the Company's Chairman, Chief Executive Officer, and the beneficial owner of approximately 70% of its outstanding common stock prior to this rights offering, Robert W. Duggan, in the principal amount of $55,000, matured and became due and the Company repaid all principal and accrued interest thereunder using a portion of the proceeds from the rights offering.

On August 11, 2021, based on a thorough review of the design and enrollment status of its two ongoing blinded Phase III Ri-CoDIFy trials, the Company announced that it combined its two blinded pivotal Phase III clinical trials evaluating ridinilazole versus vancomycin into a single study and presented this decision to the United States ("U.S.") Food and Drug Administration (the "FDA") as such. During September 2021, the Company received feedback from the FDA that the FDA did not agree with the change to the primary endpoint that the Company proposed and subsequently implemented in its ongoing Phase III Ri-CoDIFy studies when combining the trials.

On December 20, 2021, the Company announced topline results for the Phase III Ri-CoDIFy study evaluating ridinilazole, for the treatment of and Sustained Clinical Response ("SCR"), as defined below, for patients suffering from *C. difficile* infection ("*C. diff.* infection" or "CDI"). The study showed that ridinilazole resulted in a numerically higher SCR rate than vancomycin, but did not meet the study's primary endpoint for superiority. The pivotal Phase III clinical trial consisted of two Phase III clinical trials combined into a single study, designed to assess, as the primary endpoint, the superiority of ridinilazole compared to vancomycin in SCR, which is defined as clinical response of the treated episode of CDI and no recurrence of CDI through 30 days after the end of treatment. Additional endpoints included safety, tolerability, analyses of the gut microbiome and metabolome, in addition to quality of life and health economic outcome measures. We are in the process of evaluating the future path forward with respect to ridinilazole, including potential partnership opportunities.

On March 10, 2022, the Company's Chief Executive Officer, Robert W. Duggan, entered into a Note Purchase Agreement (the "2022 Note"), pursuant to which he has loaned the Company $25,000 in exchange for the issuance by the Company of an unsecured promissory note in the amount of $25,000. The 2022 Note is to accrue interest at a rate per annum equal to the prime rate as reported in the *Wall Street Journal*, which is 3.25% as of the effective date. The 2022 Note becomes due upon the earlier of (i) the consummation of a registered public offering with net proceeds of no less than $25,000 or (ii) 18 months from the date of issuance of the 2022 Note.

2. Basis of Presentation and Use of Estimates

The consolidated financial statements include the accounts of Summit Therapeutics Inc. and its wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

The consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP") and pursuant to the rules and regulations of the U.S. Securities and Exchange Commission. The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an on-going basis, management evaluates its estimates and judgments, including those related to revenue recognition, accrued research and development expenses, stock-based compensation, intangible assets, goodwill, other long-lived assets and income taxes. Management bases its estimates and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

The progression of the COVID-19 pandemic continues to evolve and its enduring impact on the Company's business remains uncertain. Management believes the estimates and assumptions underlying its financial statements are reasonable and supportable based on the information available as of December 31, 2021, however, the extent to which the COVID-19 pandemic impacts the Company's financial results beyond December 31, 2021 will depend on future developments that are highly uncertain and cannot be predicted at this time.

3. Liquidity and Capital Resources

During the year ended December 31, 2021, the Company incurred a net loss of $88,602 and cash flows used in operating activities was $72,587. As of December 31, 2021, the Company had an accumulated deficit of $299,548, cash of $71,791, research and development tax credit receivable of $15,695 and accounts receivable of $1,464. The Company expects to continue to generate operating losses for the foreseeable future. Until the Company can generate substantial revenue and achieve profitability, the Company will need to raise additional capital to fund its ongoing operations and capital needs.
Based on the Company's current funding arrangements and financial resources as of December 31, 2021, and after considering proceeds received of $25,000 from the 2022 Note issued on March 10, 2022, the Company has the ability to fund its operating costs and working capital needs for more than twelve months from the date of issuance. In order to continue to fund the operations of the Company beyond this time period, management has developed plans, which primarily consist of raising additional capital through some combination of equity or debt financings, and/or potentially entering into new collaborations. There is no assurance, however, that additional financing will be available when needed or that management of the Company will be able to obtain financing on terms acceptable to the Company. If the Company is unable to obtain funding when required

in the future, the Company could be required to delay, reduce, or eliminate research and development programs, product portfolio expansion, or future commercialization efforts, which could adversely affect its business prospects.

The accompanying consolidated financial statements are prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of the business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classifications of liabilities that might result from the outcome of this uncertainty.

4. Summary of Significant Accounting Policies

The significant accounting policies adopted by the Company in the preparation of these financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

Principles of Consolidation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”) and pursuant to the rules and regulations of the U.S. Securities and Exchange Commission. The consolidated financial statements include the accounts of Summit Therapeutics Inc. and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Foreign Currency Translation

The financial statements of the Company’s subsidiaries with functional currencies other than the U.S. dollar are translated into U.S. dollars using period-end exchange rates for assets and liabilities, historical exchange rates for stockholders’ equity and weighted average exchange rates for operating results. Translation gains and losses are included in accumulated other comprehensive (loss) income in shareholders’ equity. Foreign currency transaction gains and losses are included in other (expense) income, net in the results of operations. The Company recorded realized and unrealized foreign currency transaction (losses) gains of $(2,135) and $54 for the years ended December 31, 2021 and 2020, respectively, which is included in other (expense) income in the statements of operations and comprehensive loss.

Revenue Recognition

The Company accounts for revenue using Accounting Standards Codification ("ASC") 606 ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards.

The Company enters into out-licensing agreements within the scope of ASC 606 under which it licenses certain rights to its product candidates to third parties. Such agreements may include the transfer of intellectual property rights in the form of licenses, transfer of technological know-how, delivery of drug substances, research and development services, and participation on certain committees with the counterparty. Payments made by the customers may include one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services the Company provides through its contract manufacturers; and royalties on net sales of licensed products if they are successfully approved and commercialized. Each of these payments may result in license, collaboration, or other revenue, except revenue from royalties on net sales of licensed products, which would be classified as royalty revenue.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its out-licensing agreements, the following steps are performed: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv)

allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. Revenue is then recognized in respect of the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. As part of the accounting for these arrangements, the Company must use significant judgment to determine: (a) the performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; and (c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company also uses judgment to determine whether milestone payments or other variable consideration, except for royalties and sales-based milestones, should be included in the transaction price, as described below. The transaction price is allocated to each performance obligation based on the relative standalone selling price of each performance obligation in the contract, and the Company recognizes revenue based on those amounts when, or as, the performance obligations under the contract are satisfied.

Exclusive Licenses

If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from nonrefundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition. The measure of progress, and the resulting periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research, development and licensing arrangement. Such a change could have a material impact on the amount of revenue the Company records in future periods. Under the Company's existing license and collaboration agreements, the Company has concluded that the transfer of control to the customer occurs over the time period that the research and development services are to be provided by the Company, and this output method is, in management's judgment, the best measure of progress towards satisfying the performance obligation.

Milestone Payments

At the inception of each arrangement that includes potential research, development or regulatory milestone payments, the Company evaluates whether the milestones are considered likely to be met and estimates the amount to be considered for inclusion in the transaction price using the most-likely-amount method. If it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur, the associated milestone payment value is included in the transaction price. For milestone payments due upon events that are not within the control of the Company or the licensee, such as regulatory approvals, the Company is not able to assert that it is likely that the regulatory approval will be granted and that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur until those approvals are received. In making this assessment, the Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone. There is considerable judgment involved in determining whether it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price of the arrangement. Any such adjustments are recorded on a cumulative catch-up basis, which would affect the amounts of revenue and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments due upon first commercial sales or based on a level of sales, that are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) the occurrence of the related sales or (ii) the date upon which the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. To date, the Company has not recognized any royalty revenue from any of its licensing arrangements.

Other Operating Income

The Company generates income from government contracts that reimburse the Company for certain allowable costs for funded projects. For contracts with government agencies where the funding arrangement is considered central to the Company's ongoing operations, the Company classifies the recognized funding received as other operating income.

Income from government grants is recognized as the qualifying expenses related to the contracts are incurred, provided that there is reasonable assurance of recoverability. If the government agency approves the project proposed by the Company, the government agency funds the project upon receipt of the support for the costs incurred up to the contract limit. Income recognized upon incurring qualifying expenses in advance of billing is recorded as accrued income, a component of other current assets, in the consolidated balance sheet.

Grant income is not recognized as deductions of research and development costs because the Company acts as the principal in conducting the research and development activities and these contracts are central to its ongoing operations. The funds received through these means are held as deferred income in the consolidated balance sheets and are released to the consolidated statement of operations and comprehensive loss as the underlying expenditure is incurred and to the extent the conditions of the grant are met. The related costs incurred by the Company are included in research and development expense in the Company's consolidated statements of operations and comprehensive loss.

The Company benefits from two U.K. research and development ("R&D") tax credit cash rebate regimes: Small and Medium Enterprise ("SME") Program and the Research and Development Expenditure Credit ("RDEC") Program. Each reporting period, management evaluates which tax relief programs the Company is expected to be eligible for and records as other operating income the portion of the expense that it expects to qualify under the programs, that it plans to submit a claim for, and it has reasonable assurance that the amount will ultimately be realized. Based on criteria established by HM Revenue and Customs ("HMRC"), management of the Company expects a proportion of expenditures being undertaken in relation to its pipeline research, clinical trials management and manufacturing development activities to be eligible for the research and development tax relief programs for the year ended December 31, 2021. Qualifying expenditures largely comprise of employment costs for research staff, consumables, a proportion of relevant, permitted sub-contract costs and certain internal overhead costs incurred as part of research projects for which the Company does not receive commercial or other funding income. Credits related to the SME and RDEC Programs are recorded as other operating income in the consolidated statements of operations and other comprehensive (loss)/income. Under both schemes, the Company receives cash rebate payments of up to 33.3% of eligible research and development expenditures and these payments are not dependent on the Company's pre-tax net income levels. The Company has qualified under the more favorable SME regime for the year ended December 31, 2020 and expects to qualify under the SME regime for the year ending December 31, 2021.

Net Income Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding for the period. Diluted net loss per share is computed by dividing the diluted net loss by the weighted-average number of common shares outstanding for the period, including potentially dilutive common shares. The dilutive effect of share options and warrants are determined under the treasury stock method using the average market price for the period. In addition, the assumed proceeds under the treasury stock method include the average unrecognized compensation expense of stock options and warrants that are in-the-money.

Business Combinations

Business combinations are accounted for under the acquisition method. Acquired assets and assumed liabilities are measured at their fair values at the acquisition date. The excess of the consideration transferred over the net fair value of assets acquired and liabilities assumed is recorded as goodwill. The accounting for an acquisition involves a considerable amount of judgement and estimation. Cost, income, market or a combination of approaches may be used to establish the fair value of consideration exchanged, assets acquired, and liabilities assumed, depending on the nature of those items. The valuation approach is

determined in accordance with generally accepted valuation methods. Key areas of estimation and judgment may include the selection of valuation approaches, cost of capital, market characteristics, cost structure, impacts of synergies, and estimates of terminal value, among other factors.

While the Company uses estimates and assumptions as part of the purchase price allocation process to estimate the value of assets acquired and liabilities assumed, estimates are inherently uncertain and subject to refinement. During the measurement period, which maybe up to one year from the acquisition date, the Company may record adjustments to the assets acquired and liabilities assumed, with a corresponding offset to goodwill, to the extent that adjustments are identified to the preliminary purchase price allocation. Upon conclusion of the measurement period, or final determination of the value of the assets acquired and liabilities assumed, whichever comes first, any subsequent adjustments are recorded to results of operations. Results of operations related to business combinations are included prospectively beginning with the date of acquisition and transaction costs related to business combinations are recorded within general and administrative expenses.

Goodwill

Goodwill represents the excess of the consideration transferred over the fair value of net assets acquired. Goodwill is assigned to reporting units at the time of acquisition or when there is a change in the reporting structure and bases that allocation on which reporting units will benefit from the acquired assets and liabilities. Reporting units are defined as operating segments or one level below an operating segment, referred to as a component. The Company assesses goodwill for impairment on an annual basis or more frequently when events and circumstances occur indicating that the recorded goodwill may be impaired.

In performing the Company's annual goodwill impairment test, the Company is permitted to first assess qualitative factors to determine whether it is more likely than not that the fair value of the Company's reporting unit is less than its carrying amount, including goodwill. In performing the qualitative assessment, the Company considers certain events and circumstances specific to the reporting unit and to the entity as a whole, such as macroeconomic conditions, industry and market considerations, overall financial performance and cost factors when evaluating whether it is more likely than not that the fair value of the reporting unit is less than its carrying amount. The Company is also permitted to bypass the qualitative assessment and proceed directly to the quantitative test. If the Company chooses to undertake the qualitative assessment and concludes that it is more likely than not that the fair value of the reporting unit is less than its carrying amount, the Company would then proceed to the quantitative impairment test. In the quantitative assessment, the Company compares the fair value of the reporting unit to its carrying amount, which includes goodwill. If the fair value exceeds the carrying value, no impairment loss exists. If the fair value is less than the carrying amount, a goodwill impairment loss is measured and recorded.

As of December 31, 2021, the Company performed its annual impairment assessment of goodwill by performing a qualitative analysis for its single identified reporting unit for goodwill and determined that it is more likely than not that the fair value of the reporting unit exceeded its carrying amount.

Intangible Assets

Intangible assets include patents, licenses, an option over non-financial assets and a research and development discovery platform ("Discuva Platform").

Patents, licenses, and the option over non-financial assets are initially recorded at fair value, assigned an estimated useful life, and amortized primarily on a straight-line basis over their estimated useful lives. The Company evaluates the recoverability of its intangible and long-lived assets whenever events and changes in circumstances indicate that the carrying amount of an asset may not be fully recoverable. If events and circumstances indicate that the carrying amount may not fully be recoverable, the Company will perform a qualitative assessment, and consider certain events and circumstances specific to the intangible asset and to the entity as a whole, such as macroeconomic conditions, industry and market considerations, overall financial performance and cost factors when evaluating whether it is more likely than not that the fair value of the intangible asset is less than its carrying amount. This periodic review may result in an adjustment of estimated depreciable lives or asset impairment. When indicators of impairment are present, the carrying values of the asset are evaluated in relation to their operating performance and future undiscounted cash flows of the underlying business. If the future undiscounted cash flows are less than their carrying value, impairment exists. The impairment is measured as the difference between the carrying value and the fair

value of the underlying asset. Fair values are based on estimates of market prices and assumptions concerning the amount and timing of estimated future cash flows and assumed discount rates, reflecting varying degrees of perceived risk.

Other intangible assets are amortized in equal installments over their estimated useful lives as follows:

Intangible Asset	Amortization Period
Option over non-financial assets	Over the period of the relevant agreement

Amortization of intangible assets is included as part of the research and development expense line shown on the face of the consolidated statement of operations and comprehensive loss.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Cost comprises the purchase price plus any incidental costs of acquisition and commissioning.

Depreciation is calculated based on cost, less residual value, in equal annual installments over the estimated useful lives of the assets. The residual value, if not insignificant, is reassessed annually.

Leasehold improvements	Over the shorter of the asset's useful life or the remaining lease term
Laboratory equipment	2-10 years
Office and IT equipment	3-5 years

Depreciation is recognized as part of the general and administrative and research and development expense lines shown on the face of the consolidated statement of operations and comprehensive loss depending on the nature of the underlying assets.

Expenditures for repairs and maintenance are expensed as incurred. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations.

Leases

The Company has operating leases for real estate. The Company does not have any finance leases. Under Accounting Standards Codification 842, a contract is or contains a lease when the lessee has the right to control the use of an identified asset. The Company determines if an arrangement is a lease at inception of the contract, which is the date on which the terms of the contract are agreed to and the agreement creates enforceable rights and obligations. The lease term used to calculate the lease liability include options to extend or terminate the lease when it is reasonably certain that the option will be exercised.

At the lease commencement date, the Company measures and recognizes a lease liability and a right-of-use asset in the financial statements. Lease liabilities are recognized based on the present value of the future lease payments over the lease term at commencement date. The right-of use asset is measured by taking the present value of future lease payments, plus any incremental direct costs incurred, less any lease incentives received. As most of the Company's leases do not provide an implicit rate, the Company uses an estimated incremental borrowing rate based on the lease term and the economic environment of the lease at the lease commencement date, which is then utilized to determine the present value of future lease payments. Lease expense for minimum lease payments are recognized on a straight-line basis over the lease term, with variable lease payments recognized in the periods in which they are incurred.

The Company has existing lease agreements with lease and non-lease components, has elected to account for the lease and non-lease components as a single lease component, and has allocated all of the contract consideration to the lease component only.

Leases with an initial lease term of 12 months or less are not recorded on the balance sheet. The Company recognizes lease expense for its short-term leases on a straight-line basis over the lease term.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred to discover, research and develop product candidates, including personnel expenses, stock-based compensation expense, allocated facility-related and depreciation expenses, third-party license fees and external costs of outside vendors engaged to conduct preclinical and clinical development activities and clinical trials as well as to manufacture clinical trial materials. Non - refundable prepayments for goods or services that will be used or rendered for future research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered. Milestone and other payments made to third-parties with respect to in-process research and development, in accordance with the Company's license, acquisition and other similar agreements are expensed when determined to be probable and estimable.

The Company has entered into various research and development contracts with other companies. These agreements are generally cancellable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs or prepaid expenses where the payments made exceeds the estimated costs. When evaluating the adequacy of these balances, the Company analyzes progress of the studies, including the estimated costs to complete each study or activity, the estimation of the current stage of completion and the invoices received, as well as predetermined milestones which are not reflective of the current stage of development for prepaid expenses. Actual results could differ from the Company's estimates. In all cases, the full cost of each study or activity is expensed by the time the final report or where applicable, product, has been received. The Company's historical estimates have not been materially different from the actual costs.

Stock-Based Compensation

The Company measures and recognizes compensation expense for all stock option and restricted stock unit awards based on the estimated fair value of the award on the grant date. The Company uses the Black-Scholes option pricing model to estimate the fair value of stock option awards. The fair value is recognized as expense, over the requisite service period, which is generally the vesting period of the respective award, on a straight-line basis for each separately vesting portion of the award when the only condition to vesting is continued service. If vesting is subject to a market or performance condition, recognition is based on the derived service period of the award. Expense for awards with performance conditions is estimated and adjusted on a quarterly basis based upon the assessment of the probability that the performance condition will be met. Use of the Black-Scholes option-pricing model requires management to apply judgment under highly subjective assumptions. These assumptions include:

- Expected term—The expected term of stock options represents the weighted-average period the stock options are expected to be outstanding. The Company uses the simplified method for estimating the expected term as provided by the Securities and Exchange Commission. The simplified method calculates the expected term as the average of the time-to-vesting and the contractual life of the options.
- Expected volatility—The expected volatility was calculated based on historical volatility of the Company's share price.
- Risk-free interest rate—The risk-free rate assumption is based on the U.S. Treasury instruments, the terms of which were consistent with the expected term of the Company's stock options.
- Expected dividend—The expected dividend assumption is based on the Company's history and expectation of dividend payouts. The Company has not paid and does not intend to pay dividends.

The Company estimates expected forfeitures at the time of grant instead of accounting for forfeitures as they occur. Stock option and restricted stock unit awards have been granted at fair value to non-employees, in connection with research and consulting services provided to the Company, to non-employees in connection with corporate activities, and to employees, in connection with Stock Purchase and Restriction Agreements. Equity awards generally vest over terms of 3 or 4 years.

Income Taxes

The provision for income taxes is determined using the asset and liability approach. Tax laws may require items to be included in tax filings at different times than the items are reflected in the financial statements. A current asset or liability is recognized for the estimated taxes receivable or payable for the current year. Deferred taxes represent the future tax consequences expected to occur when the reported amounts of assets and liabilities are recovered or paid. Deferred taxes are initially recognized at enacted tax rates in force at the time of initial recognition and are subsequently adjusted for any enacted changes in tax rates and tax laws. Subsequent changes to deferred taxes originally recognized in equity are recognized in income. Valuation allowances are recorded to reduce deferred tax assets when it is more likely than not that a tax benefit will not be realized. The Company has recorded a full valuation allowance against the deferred tax assets in excess of its deferred tax liabilities, as the deferred tax liability represents future reversals of existing taxable temporary differences. The Company records interest and penalties related to income tax matters as part of income tax expense.

Concentration of Credit Risk and of Significant Supplier

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of short-term cash deposits and accounts and other receivables. The Company's cash is comprised of short-term cash deposits at a variety of financial institutions with strong credit ratings in amounts that may exceed federally insured limits and has not experienced any losses on such accounts. Cash balances maintained during the year have been principally held with reputable U.K.-based and U.S.-based banks. The Company does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The credit risk with respect to customers and funding bodies is limited as the Company has only a small number of these arrangements, including with Eurofarma, BARDA and CARB-X.

The Company relies, and expects to continue to rely, on a number of vendors to conduct its clinical trials and preclinical studies, manufacture drug product and supply clinical trial and preclinical study materials for its development programs. These programs could be adversely affected by a significant interruption in these services or the availability of materials.

Fair Value Measurements

In accordance with the provisions of fair value accounting, a fair value measurement assumes that the transaction to sell an asset or transfer a liability occurs in the principal market for the asset or liability or, in the absence of a principal market, the most advantageous market for the asset or liability and defines fair value based on the exit price model.

The fair value measurement guidance establishes a fair value hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The guidance describes three levels of inputs that may be used to measure fair value:

Level 1
Quoted prices in active markets for identical assets or liabilities as of the reporting date. Active markets are those in which transactions for the asset or liability occur in sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2
Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities. Level 2 assets and liabilities include debt securities with quoted prices that are traded less

frequently than exchange-traded instruments or securities or derivative contracts that are valued using a pricing model with inputs that are observable in the market or can be derived principally from or corroborated by observable market data.

Level 3
Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities. Level 3 assets and liabilities include financial instruments whose value is determined using pricing models, discounted cash flow methodologies, or similar techniques, as well as instruments for which the determination of fair value requires significant management judgment or estimation.

In certain cases, the inputs used to measure fair value may fall into different levels of the fair value hierarchy. In such cases, the Company categorizes such assets and liabilities based on the lowest level input that is significant to the fair value measurement in its entirety. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires judgment and considers factors specific to the asset.

Assumed Contingent Liabilities

As part of the acquisition of Discuva Limited in December 2017, the Company assumed certain contingent liabilities as certain employees, former employees and former directors of Discuva Limited are eligible for payments from Discuva Limited based on specified development and clinical milestones related to proprietary product candidates developed under the Discuva Platform. The timing of these potential payments is uncertain. The fair value of the assumed contingent liability was estimated using the expected value of the payments. The assumed contingent liabilities are subsequently measured at amortized cost using discounted cash flow models which calculate the risk adjusted net present values of estimated potential future cash flows of the payments. The assumed contingent liabilities are remeasured when there is a specific significant event that provides evidence of a significant change in the probability of successful development and clinical milestones being achieved. The models will be updated for changes in the probability of successful development and clinical milestones being achieved and other associated assumptions with the discount factor remaining unchanged within the model. A discount factor of 13% has been used to discount the contingent liabilities back to net present value. This discount factor has been calculated using appropriate measures and rates which could have been obtained in the period that the contingent liabilities were assumed. Accretion of the discount factor is recognized as part of operating expenses in the consolidated statements of operations and comprehensive loss.

Warrants

Warrants issued by the Company are recognized and classified as equity when, upon exercise, the Company would issue a fixed amount of its own equity instruments (common stock) in exchange for a fixed amount of cash or another financial asset.

Consideration received, net of incremental costs directly attributable to the issue of such new warrants, is shown in equity. Such warrants are not remeasured at fair value in subsequent reporting periods.

Warrants issued in which external services are received as consideration for equity instruments of the company should be measured at the fair value of the goods or services received. Only if the fair value of the services cannot be measured reliably would the fair value of the equity instruments granted be used. The fair value for the warrants is calculated using the Black-Scholes formula and recorded in the consolidated statement of operations and comprehensive loss on a straight-line basis over the period of the consulting services. If the services are terminated prior to the end of the consultancy agreement, the warrants cease vesting and any unvested portion of the warrants will lapse immediately.

The warrants in issue are classified within stockholders' equity as they are indexed to the Company's own shares of common stock and require settlement in its shares of common stocks with no provision for any cash settlement.

5. Recently Issued or Adopted Accounting Pronouncements

In November 2021, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2021-10, " Government Assistance (Topic 832)." This ASU increases the transparency of government assistance including the disclosure of (1) the types of assistance, (2) an entity's accounting for the assistance, and (3) the effect of the assistance on an

entity's financial statements as diversity currently exists in the recognition, measurement, presentation and disclosure of government assistance received by business entities because of the lack of specific authoritative guidance in U.S. GAAP. This ASU is effective for annual periods, and interim periods within those fiscal years, beginning after December 15, 2021. Early application of this ASU is permitted. The Company applied the amendments of this ASU to its disclosures during the fourth quarter of 2021 and the application of this ASU did not have a material impact on its financial position, results of operations or cash flows.

In October 2021, the FASB issued ASU No. 2021-08, "Business Combinations (Topic 805): Accounting for Contract Assets and Contract Liabilities from Contracts with Customers." This ASU improves the accounting for acquired revenue contracts with customers in a business combination by addressing diversity in practice and inconsistency relating to: 1) recognition of an acquired contract liability and 2) payment terms and their effect on subsequent revenue recognized by the acquirer. The amendments in this ASU require acquiring entities to apply Topic 606 to recognize and measure contract assets and contract liabilities in a business combination, whereas current U.S. GAAP requires that the acquirer measure such assets and liabilities at fair value on the acquisition date. This ASU is effective for annual periods, and interim periods within those fiscal years, beginning after December 15, 2022. The Company will apply this ASU on a prospective basis for business combinations once this ASU is effective and at that time, will be able to determine the potential impact on its financial position, results of operations or cash flows.

In May 2021, the FASB issued AS No. 2021-04, "Earnings Per Share (Topic 260), Debt - Modifications and Extinguishments (Subtopic 470-50), Compensation - Stock Compensation (Topic 718), and Derivatives and Hedging Contracts in Entity's Own Equity (Subtopic 815-40) - Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options." This ASU provides clarification and reduces diversity in an issuer’s accounting for modifications or exchanges of freestanding equity-classified written call options (such as warrants) that remain equity classified after modification or exchange. This ASU is effective for annual periods, and interim periods within those fiscal years, beginning after December 15, 2021. The Company will apply this ASU on a prospective basis for any modifications or exchanges once this ASU is effective and at that time, will be able to determine the potential impact on its financial position, results of operations or cash flows.

In December 2019, the FASB issued ASU No. 2019-12, "Income Taxes (Topic 740)." This ASU simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740. The amendments also improve consistent application and simplify U.S. GAAP for other areas of Topic 740 by clarifying and amending existing guidance. This ASU is effective for annual periods, and interim periods within those fiscal years, beginning after December 15, 2020. The Company adopted this ASU during the first quarter of 2021 and the adoption of this ASU did not have a material impact on its financial position, results of operations or cash flows.

6. Segment Reporting

The Company's chief operating decision makers (the "CODM function"), which are the Company's Chief Executive Officer and Chief Operating Officer, utilize consolidated financial information to make decisions about allocating resources and assessing performance for the entire Company. The CODM function approves of key operating and strategic decisions, including key decisions in clinical development and clinical operating activities, entering into significant contracts, such as revenue contracts and collaboration agreements and approves the Company's consolidated operating budget. The CODM function views the Company's operations and manages its business as a single reportable operating segment. The Company's single operating segment covers the Company’s research and development activities, primarily comprising the CDI program and antibiotic pipeline research activities. As the Company operates in one operating segment, all required financial segment information can be found in the consolidated financial statements.

(in thousands, except share and per share data)

The Company operates in two geographic regions: the U.K. and the U.S. The following table summarizes the Company's long-lived assets, which include the Company's property and equipment, net and right-of-use assets by geography:

	Year Ended December 31, 2021	Year Ended December 31, 2020
United Kingdom	$ 2,762	$ 1,228
United States	722	51
	$ 3,484	$ 1,279

For details of revenue from external customers by geography refer to Note 7.

7. Revenue

The following table summarizes revenue by category:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Revenue by category:		
Licensing agreements	$ 1,809	$ 860

Revenue recognized during the years ended December 31, 2021 and December 31, 2020 consists of amounts received from the Company's license and commercialization agreement with Eurofarma Laboratórios S.A.

The following table summarizes revenue by geography:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Revenue by geography:		
United States	$ —	$ —
Latin America	1,809	860
	$ 1,809	$ 860

The analysis of revenue by geography has been identified on the basis of the geographical location of each collaboration partner.

(in thousands, except share and per share data)

The following table summarizes the deferred revenue relating to Eurofarma Laboratórios S.A. and deferred other income relating to BARDA (as defined in Note 8), respectively:

	2021
Beginning deferred revenue and other income, January 1 [1]	$ 8,939
Additions	5,438
Amount of deferred revenue and other income recognized in the statement of operations	(6,438)
Ending deferred revenue and other income, December 31 [2]	$ 7,939

[1] Beginning deferred revenue and other income included $8,370 of current deferred revenue and other income and $569 of long-term deferred revenue and other income.
[2] Ending deferred revenue and other income is classified within current liabilities.

Refer to Note 8 below for further details regarding other income recognized under the BARDA contract.

Eurofarma Laboratórios S.A.

On December 21, 2017, Summit announced it had entered into an exclusive license and commercialization agreement with Eurofarma Laboratórios S.A. ("Eurofarma"), pursuant to which the Company granted Eurofarma the exclusive right to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean. The Company has retained commercialization rights in the rest of the world.

Under the terms of the license and commercialization agreement with Eurofarma, the Company received an upfront payment of $2,500 in December 2017. In February 2020, the Company reached the first enrollment milestone and earned $1,000. In September 2021, the Company reached the second enrollment milestone and earned $1,250. The terms of the contract have been assessed under ASC 606 and currently only the upfront payment and the first two enrollment milestone payments are included in the transaction price. These payments were initially reported as deferred revenue in the balance sheet and are being recognized as revenue ratably over the performance period.

Revenue recognized during the period ended December 31, 2021 was based on the transaction price that included the upfront payment and the first two enrollment milestones earned in accordance with the Company's revenue recognition policy. Revenue recognized during the period ended December 31, 2020 was based on the transaction price that included the upfront payment and the first enrollment milestone earned in accordance with the Company's revenue recognition policy. The revenue is being recognized ratably over the performance period to reflect the transfer of control to the customer occurring over the time period that the research and development services are provided by the Company. This output method is, in management’s judgment, the best measure of progress towards satisfying the performance obligation. As of December 31, 2021 and 2020, the current contract liability relating to the Eurofarma contract was $756 and $759, respectively, and was recorded in current deferred revenue in the consolidated balance sheet. As of December 31, 2021 and 2020, the non-current contract liability relating to the Eurofarma contract was $0 and $569, respectively, and was recorded in non-current deferred revenue and other income in the consolidated balance sheet.

In addition, the Company will be entitled to receive an additional $1,500 for various development milestones. The Company is also eligible to receive up to $21,400 in additional development, commercial and sales milestones when cumulative net sales equal or exceed $100,000 in the Eurofarma licensed territory. Each subsequent achievement of an additional $100,000 in cumulative net sales will result in the Company receiving additional milestone payments, which, when combined with anticipated product supply transfer payments from Eurofarma paid to the Company in connection with a commercial supply agreement to be entered into between the two parties, will provide payments estimated to range from a mid-teens to high-teens percentage of cumulative net sales in the territories where we have granted Eurofarma commercialization rights. Upon achievement of these milestones, the Company will recognize the revenues in accordance with the Company's revenue policy.

(in thousands, except share and per share data)

8. Other Operating Income

The following table sets forth the components of other operating income by category:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Other operating income by category:		
Funding income from BARDA (as defined below)	$ 4,604	$ 9,472
Research and development tax credits	15,206	9,363
Grant income from CARB-X (as defined below)	1,158	477
	$ 20,968	$ 19,312

BARDA (as defined below)

In September 2017, the Company was awarded a funding contract from the Biomedical Advanced Research and Development Authority ("BARDA"), part of the Office of the Assistant Secretary for Preparedness and Response at the United States Department of Health and Human Services, in support of the Company's Ri-CoDIFy clinical trials and clinical development of of ridinilazole.

The awarded contract was originally worth up to $62,000. In June 2019 and again in January 2020, BARDA increased the value of the contract such that it is now worth up to $72,500 and brought the total amount of committed funding to $62,400. The remaining federal government funding is dependent on BARDA in its sole discretion exercising the final independent option work segment, upon the achievement by the Company of certain agreed-upon milestones for ridinilazole. As of December 31, 2021, an aggregate of $56,492 of the total committed BARDA funding had been received and the Company has recognized $50,265 of cumulative income since contract inception.

Research and development credits

Income from tax credits, consist of R&D tax credits received in the U.K. The Company benefits from two U.K. research and development tax credit cash rebate regimes: Small and Medium Enterprise Program ("SME, Program") and the Research and Development Expenditure Credit Program ("RDEC Program"). Qualifying expenditures largely comprise of employment costs for research staff, consumables, a proportion of relevant, permitted sub-contract costs and certain internal overhead costs incurred as part of research projects for which the Company does not receive income. Tax credits related to the SME Program and RDEC Program are recorded as other operating income in the consolidated statements of operations and other comprehensive loss. Under both schemes, the Company receives cash payments that are not dependent on the Company’s pre-tax net income levels.

Based on criteria established by Her Majesty’s Revenue and Customs ("HMRC"), a portion of expenditures being carried out in relation to the Company's pipeline research and development, clinical trials management and third-party manufacturing development activities are eligible for the SME regime and the Company expects such elements of expenditure will also continue to be eligible for the SME regime for future periods.

As of December 31, 2021 and 2020, the current research and development tax credit receivable was $15,695 and $9,856, respectively.

(in thousands, except share and per share data)

CARB-X (as defined below)

In May 2021, the Company announced the selection of a new preclinical candidate, SMT-738, from the DDS-04 series for development in the fight against multi-drug resistant infections, specifically Carbapenem-resistant Enterobacteriaceae ("CRE") infections. Simultaneously, the Company announced it had received an award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program ("CARB-X") to progress this candidate through preclinical development and Phase Ia clinical trials. The award commits initial funding of up to $4,100, with the possibility of up to another $3,700 based on the achievement of future milestones. As of December 31, 2021, $485 of grant funding from CARB-X has been received, $96 is in accounts receivable for amounts billed, $574 is in other current assets as a contract asset and the Company has recognized $1,155 of cumulative income since contract inception.

Grant income recognized during the year ended December 31, 2021 relates to SMT-738. Grant income recognized during the year ended December, 31, 2020 consists of income from a sub-award from CARB-X for the Company's antibiotic pipeline research and development activities specifically relating to the DDS-01 series of antibiotics, targeting Neisseria gonorrhoeae, or N. gonorrhoeae, using the Discuva Platform. In the fourth quarter of 2020, the Company decided not to advance the DDS-01 series and to cease work on the gonorrhoeae program, and as such, no further grant income has been received from CARB-X under this sub-award.

9. Other (Expense) Income

The following table sets forth the components of other (expense) income:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Foreign currency (loss) gain	$ (2,135)	$ 54
Remeasurement of liabilities [1]	—	480
Interest income	—	4
Interest expense	(281)	(255)
	$ (2,416)	$ 283

[1] Remeasurement of liabilities during the year ended December 31, 2020, relates to a revaluation of assumed contingent liabilities for potential payments to certain employees, former employees and former directors of Discuva Limited, based on specified development and clinical milestones related to proprietary product candidates developed under the Discuva Platform (see Note 16 for further details).

10. Income Tax

The components of the Company's loss before income taxes are as follows:

	Year Ended December 31, 2021	Year Ended December 31, 2020
United Kingdom	$ (72,244)	$ (51,197)
United States	(16,358)	(1,713)
Loss before income taxes	$ (88,602)	$ (52,910)

(in thousands, except share and per share data)

Significant components of the provision for income taxes are as follows:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Current income tax benefit:		
Federal United States	$ —	$ (215)
State - United States	—	2
Non-United States	—	—
Total	—	(213)
Federal - United States	—	—
State - United States	—	—
Non-United States	—	—
Total deferred tax	—	—
Total income tax benefit	$ —	$ (213)

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes.

The major components of deferred tax assets and liabilities are as follows:

	December 31, 2021	December 31, 2020
Deferred tax assets:		
Net operating loss carryforward	$ 49,422	$ 29,831
Research and development credit carryforward	941	—
Stock based compensation	2,560	1,167
Other	1,477	491
Total deferred tax assets	54,400	31,489
Deferred tax liabilities:		
Intangible asset	(2,600)	(2,189)
Other	(54)	(71)
Total deferred tax liabilities	(2,654)	(2,260)
Net deferred tax assets before valuation allowance	51,746	29,229
Valuation allowance	(51,746)	(29,229)
Deferred tax, net	$ —	$ —

For the year ended December 31, 2021 and 2020, the Company recorded a deferred tax asset of $54.400 and $31,489 respectively. The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets, which are comprised primarily of net operating loss carryforwards and excess tax benefits related to stock-based compensation. Management has considered the Company's history of cumulative net losses in the United States ("U.S.") and the United Kingdom ("U.K."), estimated future taxable income, as well as prudent and feasible tax planning strategies, and has concluded that it is more likely than not that the Company will not realize the benefits of its U.S. federal and state deferred tax

assets and U.K. deferred tax assets. Accordingly, a full valuation allowance has been established against these net deferred tax assets as of December 31, 2021 and 2020, respectively. The Company reevaluates the positive and negative evidence at each reporting period. The Company's valuation allowance increased during 2021 by $22,517 primarily due to the generation of net operating loss and stock-based compensation.

As of December 31, 2021 and 2020, the Company had U.S. Federal net operating loss carryforwards of approximately $1,034 and $232, respectively, which may be available to offset future income tax liabilities. The 2017 Tax Cuts and Jobs Act (" TCJA") will generally allow losses incurred after 2017 to be carried over indefinitely, but will generally limit the net operating loss deduction to the lesser of the net operating loss carryover or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended). In addition, the Company has approximately $165 in U.S. State loss carryforwards which expire through various dates through 2040 and as of December 31, 2021, the Company had an estimated U.S. federal research and development tax credit carryforwards of $941 which may be available to offset future tax liabilities, and each begin to expire in 2033. The Company also had approximately $191,714 in U.K. loss carryforwards available to use against future taxable profits on a year-by-year basis (a potential deferred tax asset of $47,929). To the extent that U.K. taxable profits exceed £5,000 in each year, the loss available to utilize against profits in excess of £5,000 will be restricted to 50%. The U.K. loss carryforwards do not lapse and therefore, the full amount will be relieved over time provided there are sufficient profits against which the losses can be utilized.

Utilization of the U.S. net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not completed a study to assess whether a change of ownership has occurred, or whether there have been multiple ownership changes since its formation. Any limitation may result in the loss of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization.

U.K. tax losses are subject to additional restrictions where there is a change in ownership in the business and certain other conditions are met. An ownership change of a UK tax resident company would occur where (directly or indirectly) a single person acquires more than half of the ordinary share capital of a company, or two or more persons each acquire a holding of at least 5% of the ordinary share capital of a company and these holdings together amount to more than half the ordinary share capital of a company. Where a change in ownership has occurred, and within three years prior to that change in ownership and five years afterwards, there is a major change in the nature and conduct of trade of that company or the trade of that business becomes small or negligible, any losses carried forward will be extinguished from the point of the change in ownership. In addition, losses accrued subsequent to April 1, 2017 will be extinguished on a change of ownership when there is a major change in the nature or conduct of a company's business, or where there is a major change in the scale of that business, or a company ceases to carry on a particular trade or business. The Company has not completed a study to assess whether a change of ownership has occurred since its formation, or whether there has been a major change in the Company's business that would restrict the U.K. tax losses. Any limitation may result in the loss of a portion of the net operating loss carryforwards before utilization.

The 2017 Tax Cuts and Jobs Act ("2017 Act") created a requirement that US corporations include in income earnings of certain controlled foreign corporations ("CFC") under the global intangible low taxed income ("GILTI") regime. Pursuant to the FASB Staff Q&A, Topic 740 No.5. Accounting for Global Intangible Low-taxed Income, the Company is allowed to make an accounting policy election to either recognize deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as period expense only. The Company has elected to account for GILTI in the year the tax is incurred and include the current tax impact of GILTI in the effective tax rate. Given the Company's loss position in the U.S. and the valuation allowance recorded against its U.S. net deferred tax assets, these provisions have not had a material impact on the Company's consolidated financial statements.

On March 27, 2020, the United States enacted the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"). The Cares Act includes provisions relating to refundable payroll tax credits, deferment of the employer portion of certain payroll taxes, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction

(in thousands, except share and per share data)

limitations, and technical corrections to tax depreciation methods for qualified improvement property. The CARES Act also established a Paycheck Protection Program whereby certain small businesses are eligible for a loan to fund payroll expenses, rent, and related costs.

The Company considered the provisions under the CARES Act and elected not to take advantage of the provisions of the CARES Act as the effect of such provisions was not expected to have a material impact on the Company's results of operations, cash flows, and consolidated financial statements.

During 2021, the U.K. Government announced that from April 1, 2023, the corporation tax rate would increase to 25%. This new law was enacted on June 10, 2021. The overall effect of the change was an increase in net deferred tax assets by $9,311 and an increase in valuation allowance by an equal amount.

A reconciliation of the Company's effective tax rate to the U.S. federal statutory rate is as follows:

	Year Ended December 31, 2021	Year Ended December 31, 2020
U.S. federal income tax statutory rate	21.0 %	21.0 %
Change in valuation allowance	(10.5)%	(12.1)%
Non-deductible expenses	(0.4)%	(3.9)%
Refundable research and development tax credit	(8.3)%	(7.0)%
Effect of foreign operations taxed at various rates	0.5 %	0.9 %
Stock-based compensation	(1.6)%	— %
Other	(0.7)%	1.4 %
	— %	0.30 %

In the U.K., the Company is entitled to a research and development tax relief for small and medium-sized enterprises which allows the Company an enhanced deduction rate of 230% on qualifying research and development expenditure (the tax relief). If the Company incurs tax losses, it is entitled to surrender the lesser of unrelieved tax loss sustained and the tax relief. As the realization of the tax relief does not depend on generation of future taxable income or the Company's ongoing tax status or tax position, the Company does not consider the tax relief as an element of income tax accounting under ASC 740. For the year ended December 31, 2021 and 2020, the Company recognized research and development tax relief of $15,206 and $9,363 respectively, which is included in other operating income in the consolidated statements of operations and other comprehensive loss.

It is the intention of the Company to reinvest the earnings of its non-U.S. subsidiaries in those operations and not to repatriate the earnings to the U.S. Accordingly, the Company does not provide for deferred taxes on differences between financial reporting and tax basis in its investments in foreign subsidiaries as they are considered permanent in duration or are not expected to reverse in the foreseeable future.

The Company does not have any uncertain tax positions as of December 31, 2021. In the U.K., tax returns for the year ended December 31, 2020 remains subject to examination by HMRC.

In the U.S., the Company files income tax returns in various states. In the U.S., tax years from 2018 remain subject to examination by the U.S. Internal Revenue Service and state tax authorities. The Company is not currently under examination by the Internal Revenue Service or any other jurisdiction for years 2018 through present. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. The Company's policy is to recognize interest and penalties related to uncertain tax positions as part of its income tax provision. As of December 31, 2021, and 2020, the

(in thousands, except share and per share data)

Company has recorded no liability for unrecognized tax benefits, interest, or penalties related to federal, state or foreign income tax matters.

11. Loss per Share

The following table sets forth the computation of basic and diluted net loss per share:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Net loss	$ (88,602)	$ (52,697)
Basic weighted average number of shares of common stock outstanding	92,239,306	69,524,148
Diluted weighted average number of shares of common stock outstanding	92,239,306	69,524,148
Basic net loss per share	$ (0.96)	$ (0.76)
Diluted net loss per share	$ (0.96)	$ (0.76)

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding for the period. Diluted net loss per share is computed by dividing the diluted net loss by the weighted-average number of common shares outstanding for the period, including potentially dilutive common shares. The dilutive effect of share options and warrants are determined under the treasury stock method using the average market price for the period. In addition, the assumed proceeds under the treasury stock method include the average unrecognized compensation expense of stock options and warrants that are in-the-money. Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods, as the inclusion of all potential common share equivalents outstanding would have been anti-dilutive.

The following potentially dilutive securities were excluded from the computation of the diluted net loss per share of common stock for the periods presented because their effect would have been anti-dilutive:

	2021	2020
Restricted stock units	—	26,923
Options to purchase common stock	13,797,556	3,672,968
Warrants	5,821,137	5,821,137
Shares expected to be purchased under employee stock purchase plan	202,045	—
	19,820,738	9,521,028

12. Goodwill and Intangible Assets

Goodwill

Goodwill is measured as the excess of the cost of the acquisition over the sum of the amounts assigned to tangible and identifiable intangible assets acquired less liabilities assumed. The Company assigns assets acquired (including goodwill) and liabilities assumed to one or more reporting units as of the date of acquisition. Typically acquisitions related to a single reporting unit do not require the allocation of goodwill to multiple reporting units. If the products obtained in an acquisition are assigned to multiple reporting units, the goodwill is distributed to the respective reporting units as part of the purchase price allocation process.

(in thousands, except share and per share data)

Goodwill and purchased intangible assets are reviewed for impairment annually during the fourth quarter of each fiscal year and whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. The process of evaluating the potential impairment of goodwill and intangible assets requires significant judgment. The Company regularly monitors current business conditions and other factors including, but not limited to, adverse industry or economic trends and lower projections of profitability that may impact future operating results.

The Company's annual evaluation for impairment of goodwill consists of one reporting unit. In accordance with the Company's policy, the Company completed its annual evaluation for impairment in the fourth quarter of 2021 using the qualitative assessment. No impairment charge was recognized for the year ended December 31, 2021 and there have been no cumulative goodwill impairment charges recognized to date.

As of December 31, 2021 and 2020, goodwill was $2,009 and $2,030, respectively and represents goodwill recognized from the acquisition of Discuva Limited in December of 2017. Changes year over year are the result of foreign currency movements.

Intangible Assets

Components of the Company's acquired intangible assets are comprised of the following:

	December 31, 2021		
	Gross	Accumulated amortization and impairment charges	Net
Utrophin program acquired	$ 4,487	$ (4,487)	$ —
Discuva platform acquired	14,416	(4,017)	10,399
Option over non-financial asset	912	(912)	—
Other patents and licenses	148	(148)	—
	$ 19,963	$ (9,564)	$ 10,399

	December 31, 2020		
	Gross	Accumulated amortization and impairment charges	Net
Utrophin program acquired	$ 4,534	$ (4,534)	$ —
Discuva platform acquired	14,565	(3,050)	11,515
Option over non-financial asset[(1)]	921	(921)	—
Other patents and licenses	150	(150)	—
	$ 20,170	$ (8,655)	$ 11,515

[(1)]During the year ended December 31, 2020, management identified an impairment related to the option over non-financial asset pursuant to an Evaluation and Option Agreement with a collaboration partner. The partner is no longer conducting antibiotic candidate programs over which the Company had the option, management therefore determined that the fair value of the option to acquire the assignment of the proprietary rights for antibiotic candidates is $0. Accordingly, the asset was written off in its entirety resulting in an impairment charge of $859 recognized in operating expenses.

Amortization expense was $1,017 and $1,250 for the years ended December 31, 2021 and 2020, respectively. The weighted-average remaining life at December 31, 2021 for our Discuva platform intangible asset was approximately 10.4 years.

(in thousands, except share and per share data)

The estimated net amortization expense related to acquired intangible assets for future years is:

	Amount
2022	$ 999
2023	$ 999
2024	$ 999
2025	$ 999
2026	$ 999
Thereafter	$ 5,404

13. Property and Equipment

Property and equipment consisted of the following:

	December 31, 2021	December 31, 2020
Laboratory equipment	$ 2,626	$ 759
Furniture and fixtures, office equipment and software	1,081	804
Leasehold improvements	364	291
Property and equipment, gross	4,071	1,854
Less: accumulated depreciation	3,377	1,129
Property and equipment, net	$ 694	$ 725

Depreciation expense for the years ended December 31, 2021 and 2020 was $330 and $302, respectively.

14. Research and Development Prepaid Expenses and Accrued Liabilities

Included within prepaid expenses at December 31, 2021 and 2020 is $6,138 and $8,490, respectively, of prepayments relating to research and development expenditures. Included within accrued liabilities at December 31, 2021 and 2020 is $5,226 and $1,502, respectively, relating to research and development expenditures.

These amounts are determined based on the estimated costs to complete each study or activity, the estimation of the current stage of completion and the invoices received, as well as predetermined milestones which are not reflective of the current stage of development for prepaid expenses. However, prepaid expenses decrease and accrued liabilities increase as the activities progress, and if actual costs incurred exceed the prepaid expense, an accrual will be recorded for the liability. The key sensitivity is the estimated current stage of completion of each study or activity, which is based on information received from the supplier and the Company's operational knowledge of the work completed under those contracts.

15. Leases

The Company has operating leases for real estate. The Company does not have any finance leases.

During the year ended December 31, 2021, the Company recorded $3,389 of additional right-of-use assets of which $2,359 related to two new leases that commenced during the period for its Menlo Park, California, U.S. and Sawston, U.K. locations and $1,030 which related to one lease that was extended during the period for its Oxfordshire, U.K location.

The carrying value of the right-of-use assets as of December 31, 2021 and 2020 is $2,790 and $554, respectively.

(in thousands, except share and per share data)

The elements of lease expense were as follows:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Lease Cost:		
Fixed lease costs	$ 785	$ 478
Variable lease costs	164	171
Short-term lease	278	272
Total lease cost	$ 1,227	$ 921

The weighted average discount rate and the weighted average remaining lease term were 2.5% and 3.9 years, respectively, as of December 31, 2021. The weighted average discount rate and the weighted average remaining lease term were 3.75% and 1.1 years, respectively, as of December 31, 2020.

Future lease payments under non-cancelable leases as of December 31, 2021 are detailed as follows:

Year Ending December 31,	Amount
2022	$ 1,037
2023	509
2024	508
2025	508
2026	386
Total lease payments	2,948
Less: imputed interest	166
Total operating lease liabilities	$ 2,782

Total operating lease liabilities balance sheet presentation:	
Current lease liabilities	$ 1,091
Non-current lease liabilities	1,691
	$ 2,782

Amounts presented above do not include payments related to the Company's Cambridge, Massachusetts, United States office where the lease term is month to month and therefore was not capitalized on the balance sheet.

16. Other Non-Current Liabilities

Included within other non-current liabilities at December 31, 2021 and 2020 is $2,531 and $2,263, respectively, relating to assumed contingent liabilities. As part of the acquisition of Discuva Limited in December 2017, the Company assumed certain contingent liabilities as certain employees, former employees and former directors of Discuva Limited are eligible for payments from Discuva Limited based on specified development and clinical milestones related to proprietary product candidates developed under the Discuva Platform. The timing of these potential payments is uncertain.

The contingent liability was remeasured in the third quarter of 2020 to reflect a change in the timing of expected payments following the Company's decision not to advance the DDS-01 series of antibiotics and to cease work on the gonorrhoeae program. The gain on the remeasurement of the liability recognized during the year ended December 31, 2020 of $480 is included within other (expense) income in the consolidated statements of operations and comprehensive loss. There were no remeasurement losses or gains recognized during the year ended December 31, 2021.

17. Stockholders' Equity

Reverse Stock Split

In conjunction with the Company's Redomiciliation Transaction in (as defined in Note **1**), the Company acquired all of the outstanding ordinary shares of Summit Therapeutics plc on the basis of one share of the Company's common stock for every 5 ordinary shares outstanding, which had the effect of a 1-for-5 reverse stock split. On the effective date of the Redomiciliation, the number of outstanding shares was reduced from 336,159,511 to 67,231,903. All share and per share amounts in these consolidated financial statements and related notes for periods prior to the Redomiciliation Transaction have been retroactively adjusted to reflect the effect of the exchange ratio.

Common Stock

On May 12, 2021, the Company closed its rights offering, which was fully subscribed and received aggregate gross proceeds of $75,000 from the sale of 14,312,976 shares of common stock to existing investors at a price per share of $5.24. Offering costs of $159 were incurred. In connection with the closing of the rights offering, the Second Note (see Note 20) matured and became due and the Company repaid all principal and accrued interest thereunder using a portion of the proceeds from the rights offering.

On November 6, 2020 the Company completed a private placement of its common stock and received gross proceeds of $50,000 from the issuance and sale of 14,970,060 shares of common stock to Mr. Robert W. Duggan and two other existing shareholders of the Company at a price of $3.34 per share. Offering costs of $48 were incurred.

On December 24, 2019, the Company completed a private placement of its common stock, and received aggregate gross proceeds of $50,000 from the issuance and sale of 35,075,690 shares of common stock to existing investors at a price of $1.43 per share. Offering costs of $912 were incurred.

Warrants

As part of the private placement on December 24, 2019, the participating investors were granted warrants with the right to subscribe for 5,261,350 shares of common stock at an exercise price of $1.58, exercisable any time in the period commencing on the date falling six months following December 24, 2019 and ending on the tenth anniversary of admission. Each warrant entitles the warrant holder to subscribe in cash for one share. Shares of common stock allotted pursuant to the exercise of the warrant will rank in full for all dividends and other distributions with a record date after the exercise date with the shares of common stock in issue at that date. The Company has the option to require the warrant holder to exercise some or all of the outstanding warrants after the third anniversary date if the ten-day volume weighted average price of the shares of common stock as reported on Nasdaq represents a premium of at least 50 percent to the exercise price. The warrants are classified within stockholders' equity as they are indexed to the Company's shares of common stock and require settlement in its shares of common stock with no provision for any cash settlement.

Also, as part of the private placement on December 24, 2019, certain consultants were granted warrants with the right to subscribe for 3,358,732 shares of common stock in exchange for certain services. The warrants have an exercise price of $1.44 and vest quarterly over three years. If the consulting agreement terminated prior to three years after the date of the grant, all unvested warrants will be deemed cancelled. On June 30, 2020, the consulting agreement was terminated and 2,798,945 warrants cancelled immediately. The remaining 559,787 of outstanding warrants are held by Dr. Maky Zanganeh and Dr. Elaine Stracker (see Note 20).

Warrants granted over shares of common stock to consultants in exchange of certain services are similar to stock-based compensation (see Note 18). The Company had 5,821,137 total warrants outstanding as of December 31, 2021 and 2020, respectively, and an intrinsic value of $6,559 as of December 31, 2021 and $18,260 as of December 31, 2020.

Dividends

The Company has never declared or paid cash dividends on its shares of common stock or on Summit Therapeutics plc's ordinary shares. The Company currently intends to retain all of its future earnings to fund the development and expansion of its business.

18. Stock-Based Compensation

2016 Long Term Incentive Plan

In September 2020, in conjunction with the Redomiciliation, the 2016 Long Term Incentive Plan, (the "2016 Plan") and the Company's outstanding restricted stock units ("RSUs") were assumed and adopted by Summit Therapeutics Inc., and all awards were exchanged with replacement awards issued. Subsequent to the Redomiciliation, no additional grants will be made under the 2016 Plan and any outstanding awards under the 2016 Plan and RSUs will continue with their original terms. The Company concluded that the adoption of the 2016 Plan and RSUs and issuance of replacement awards was a modification but with no change in the material rights and preferences and therefore, no recorded change in the fair value of each respective award is needed.

2020 Stock Award Plan

In September 2020, the Company's Board of Directors approved the 2020 Stock Incentive Plan (the "2020 Plan"), which became effective on September 21, 2020. The 2020 plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. Upon the effectiveness of the 2020 Plan, the Company ceased granting awards under its 2016 Plan.

A total of 8,000,000 shares of common stock were initially reserved for issuance under the 2020 Plan. Additionally, up to 5,000,000 shares of common stock, including RSUs can be added to the 2020 Plan for future issuance from options that expire, lapse unexercised or are terminated from the 2016 Plan or any other predecessor plans. The number of shares of common stock that may be issued under the 2020 Plan will automatically increase on each January 1, beginning in 2021 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2030, equal to the lesser of (i) 6,400,000 shares of common stock, (ii) 4% of the common shares outstanding on the final day of the immediately preceding calendar year and (iii) an amount as determined by the Company's Board of Directors. As of December 31, 2021, there are 2,293,700 shares available to be issued under the 2020 Plan.

2020 Employee Stock Purchase Plan

The 2020 Employee Stock Purchase Plan (the "2020 ESPP") was adopted by the Board of Directors and approved by the Company's shareholders on July 17, 2020 and approved by the predecessor company shareholders on August 19, 2020. The 2020 ESPP initially authorized the issuance of up to 1,000,000 shares of common stock to participating employees. The number of common shares that may be issued under the 2020 ESPP automatically increases on each fiscal year commencing January 1, 2021 and continuing for each fiscal year until, and including the fiscal year commencing on, January 1, 2030 equal to the least of (i) 1,600,000 shares of common stock, (ii) 1% of the common shares outstanding on such date and (iii) an amount as determined by the Company's Board of Directors. As of December 31, 2021, there were 1,825,750 shares available to be issued under the 2020 ESPP.

The first offering period of the 2020 ESPP plan consists of seven months, commenced on August 2, 2021 and will terminate on February 28, 2022. Offering periods thereafter will be six months in duration and will commence immediately proceeding the end of the previous offering period, unless otherwise determined by the Board of Directors or Compensation Committee. The next offering period commenced on March 1, 2022. Under the 2020 ESPP, eligible employees can purchase shares of common stock through payroll deductions of up to 15% of their compensation received during the plan period or such shorter period during which deductions from payroll are made, up to a defined maximum amount. The option price is determined based on the lesser of the closing price of common stock on (i) the first business day of the plan period or (ii) the exercise date, or shall be based solely on the closing price of the common stock on the exercise date; provided that such option price shall be at least 85% of the applicable closing price. In the absence of a determination by the Board of Directors or the Compensation Committee, the

(in thousands, except share and per share data)

option price is 85% of the lesser of the closing price of the common stock on (i) the first business day of the plan period or (ii) the exercise date.

The closing price is the (a) the closing price (for the primary trading session) on the Nasdaq Global Select Market or (b) the average of the closing bid and asked prices in the over-the-counter-market, whichever is applicable, as published in the *Wall Street Journal* or another source selected by the Board or the Committee.

Stock Option Valuation

The Company estimates the fair value of stock options granted to employees and directors using the Black-Scholes valuation model. Stock options granted under the 2016 and 2020 Plans generally vest over three or four years and expire after ten years. This valuation methodology utilizes several key assumptions as highlighted below.

The assumptions used in the Company's valuation are summarized as follows, presented on a weighted average basis:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Risk-free interest rate	1.05 %	0.29 %
Expected term (in years)	5.7	5.9
Expected volatility	74.5 %	71.9 %
Expected annual dividends per share	— %	— %

The following table summarizes the Company's stock option activity for the year ended December 31, 2021:

	Number of share options	Weighted average exercise price	Weighted average remaining contractual term	Aggregate intrinsic value
Outstanding as of December 31, 2020	3,672,968	$ 2.90	8.9 years	$ 6,641
Granted	13,262,016	$ 5.76		
Forfeited	(2,012,851)	$ 3.61		
Exercised	(1,124,577)	$ 2.74		
Outstanding as of December 31, 2021	13,797,556	$ 5.55	8.6 years	$ 712
Outstanding as of December 31, 2021 - vested and expected to vest	12,685,817	$ 5.51	8.6 years	$ 709
Exercisable at December 31, 2021	1,598,709	$ 3.60	7.2 years	$ 406

The weighted-average grant-date fair value of stock options granted during the years ended December 31, 2021 and 2020 was $3.50 and $2.20, per share, respectively.

The aggregate intrinsic value of stock options exercised during the years ended December 31, 2021 and December 31, 2020 was $3,744 and $857, respectively. The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company’s common stock for those stock options that had exercise prices lower than the fair value of the Company’s common stock.

As of December 31, 2021, total unrecognized compensation cost related to unvested stock option grants was approximately $27,905. This amount is expected to be recognized over a weighted average period of approximately 2.2 years.

(in thousands, except share and per share data)

In September 2021, the Compensation Committee of the Board of Directors approved a modification to the Company's outstanding performance-based stock option awards for active employees which removed the performance-based vesting criteria from these awards. Following this modification, the option awards are subject only to previously existing time-based vesting conditions. The Company accounted for this change as a modification in accordance with the requirements of Accounting Standards Codification Topic 718. As a result, 9,250,000 options, related to twenty-five employees, that were previously authorized that had not achieved a grant date became granted on September 24, 2021 relating to the modification. The Company will recognize the newly assessed measurement date fair value of the awards as compensation expense over the remaining vesting period. The incremental compensation expense related to the modification for the year ended December 31, 2021 was $4,872. The stock option activity above incorporates the modified awards.

Restricted Stock Units

The Company's outstanding restricted stock units ("RSUs") consist of nominal-cost options which were granted to non-executive directors. The following table summarizes the activity relating to RSUs for the year ended December 31, 2021:

	Number of Shares	Weighted Average Grant Date Fair Value
RSUs - beginning of period	26,923	$ 1.60
Vested	(26,923)	$ 1.60
RSUs - end of period	—	$ —

The aggregate intrinsic value of restricted stock units vested during the years ended December 31, 2021 and December 31, 2020 was $125, respectively.

Warrants

The fair value of warrants is estimated on the date of grant using the Black-Scholes valuation methodology. Expected volatilities are based on historical share price performance, weighted to exclude periods of unusually high volatility. The Company assumed the warrants to be exercised immediately on vesting. The risk-free rate is equal to the prevailing U.K. Gilts rate at grant date that most closely matches the expected term of the grant, as the warrants were issued prior to the Redomiciliation. Expected dividend yield is zero, and consistent with the Board of Directors' view that the Company's business model is to generate value through capital growth rather than the payment of dividends.

Each warrant entitles the warrant holder to subscribe in cash for one share. Shares of common stock allotted pursuant to the exercise of the warrant will rank in full for all dividends and other distributions with a record date after the exercise date with the shares of common stock in issue at that date.

As of December 31, 2021, 5,821,137 warrants were granted, of which 559,787 warrants were granted to consultants and 5,261,350 warrants were granted to investors (refer to Note 20 for further details). All warrants are considered vested at December 31, 2021, have a weighted-average exercise price of $1.56, an aggregate intrinsic value of $6,559, and a weighted average remaining contractual life of 4.0 years.

At December 31, 2021, there was no unrecognized compensation expense related to warrants.

(in thousands, except share and per share data)

Stock-Based Compensation

Stock-based compensation expense related to stock options is recorded within the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Research and development	$ 5,909	$ 749
General and administrative	6,895	1,017
Total stock-based compensation	$ 12,804	$ 1,766

19. Commitments and Contingencies

Fixed asset purchase commitments

At December 31, 2021 and 2020, the Company had no capital commitments.

Other commitments

The Company enters into contracts in the normal course of business with various third parties for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. Most contracts provide for termination upon notice, and therefore are cancellable contracts. As of December 31, 2021, total contractual commitments are estimated to be approximately $17,046 and the majority of these commitments are due within one year.

Indemnifications

The Company's certificate of incorporation provides that it will indemnify the directors and officers to the fullest extent permitted by Delaware law. In addition, the Company has entered into indemnification agreements with all of the directors and executive officers. These indemnification agreements may require the Company, among other things, to indemnify each such director or executive officer for some expenses, including attorneys' fees, judgments, fines, and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of the Company's directors or executive officers. The Company believes the fair value for these indemnification obligations is minimal. Accordingly, the Company has not recognized any liabilities relating to these obligations as of December 31, 2021.

Legal Proceedings

The Company is not currently subject to any material legal proceedings.

20. Related Party Transactions

On December 6, 2019, the Company entered into a deed of termination of the relationship agreement with Mr. Robert W. Duggan and Cairn Financial Advisers LLP, a limited liability partnership incorporated in England and Wales with the Registrar of Companies of England and Wales, as the Company's nominated adviser. The relationship agreement regulated the Company's relationship with Mr. Robert W. Duggan and limited Mr. Robert W. Duggan's influence over the Company's corporate actions and activities and the outcome of general matters pertaining to the Company. The deed of termination became effective on February 24, 2020, upon the cancellation of the admission of the ordinary shares on the Alternative Investment Market, a sub-market of the London Stock Exchanges.

December 24, 2019 Private Placement

On December 24, 2019, the Company completed a private placement of its common stock and received aggregate gross proceeds of $50,000 from the issuance and sale of 35,075,690 shares of common stock at a price of $1.43 per share, of which 33,231,410 shares of common stock were subscribed by Mr. Robert W. Duggan. Also, as part of the private placement,

participating investors were granted warrants with the right to subscribe for 5,261,350 shares of common stock at an exercise price of $1.58, of which 4,984,711 were granted to Mr. Robert W. Duggan at an exercise price of $1.43 per share for a subscription share plus a subscription warrant, pursuant to a securities purchase agreement he entered into with the Company.

In conjunction with the December 24, 2019 private placement, 90,495 shares of common stock were subscribed by Mr. Glyn Edwards, the Company's former Chief Executive Officer. Also as part of this private placement, Mr. Glyn Edwards was granted warrants with the right to subscribe for 13,574 shares of common stock at an exercise price of $1.43 per share for a subscription share plus a subscription warrant, pursuant to a securities purchase agreement he entered into with the Company.

November 6, 2020 Private Placement

On November 6, 2020 the Company completed a private placement of its common stock and received gross proceeds of $50,000 from the issuance and sale of 14,970,060 shares of common stock at a price of $3.34 per share, of which 14,071,856 shares of common stock were subscribed by Mr. Robert W. Duggan.

In conjunction with the November 6, 2020 private placement, 149,701 shares of common stock were subscribed by the Mahkam Zanganeh Revocable Trust. Dr. Maky Zanganeh was appointed to the Board of Directors on November 11, 2020 and became the Company's Chief Operations Officer on November 22, 2020. As trustee of the Mahkam Zanganeh Revocable Trust, Dr. Maky Zanganeh is deemed to beneficially own the securities of the Company held by the Mahkam Zanganeh Revocable Trust.

Consultancy Agreements

In 2020, the Company had in place a consultancy agreement with Dr. Maky Zanganeh and Associates, Inc. (“MZA”) to provide support for clinical operation activities related to the global Phase III clinical program. Dr. Maky Zanganeh is the sole owner of MZA, and Dr. Elaine Stracker, who served for a period during fiscal year 2020 as a director of the Company and as the Company’s Interim Chief Operations Officer, was at the time the General Counsel and Senior Vice President for Corporate Development at MZA. The fees for such services under the consultancy agreement with MZA were $75 per month. In addition to such monthly fee, MZA was granted warrants over 3,358,732 shares of common stock with an exercise price of $1.44 per share, vesting on a quarterly basis over three years from the date of grant, subject to MZA’s provision of consultancy services to the Company during such period. During the period of MZA's engagement, $470 of consultancy fees were incurred by the Company and a warrant expense of $512 was recognized. The consultancy agreement with MZA was terminated by mutual agreement on June 30, 2020. The warrants granted to MZA were subsequently assigned to Dr. Maky Zanganeh and Dr. Elaine Stracker. Dr. Maky Zanganeh and Dr. Elaine Stracker have vested warrants to purchase 489,815 and 69,972 shares of common stock, respectively, which can be exercised through June 30, 2025.

March 24, 2021 Note Purchase Agreement

On March 24, 2021, Mr. Robert W. Duggan, entered into a Note Purchase Agreement (the “Initial Purchase Agreement”) pursuant to which he has loaned the Company $55,000 in exchange for the issuance by the Company of an unsecured promissory note (the “Initial Note”) in the amount of $55,000. The Initial Note was to accrue interest at a rate per annum equal to 150% of the applicable 10 Year U.S. Treasury rate, as adjusted monthly. The rate is initially estimated to be approximately 2.4%. The terms of the Initial Note were that it would mature and become due upon the earlier of (i) the consummation of a registered public offering with net proceeds of no less than $55,000, or (ii) 13 months from the date of issuance of the Initial Note. On April 20, 2021, the Company determined, with Mr. Duggan’s agreement, to rescind both the Initial Purchase Agreement and the Initial Note issued thereunder, and repaid the principal amount of the Initial Note in full, without interest or penalty, as such for the year ended December 31, 2021, the Company recognized imputed interest of $103 within additional paid in capital. For the year ended December 31, 2021, debt issuance costs recognized related to the Initial Note were immaterial.

March 26, 2021 Sublease Agreement with Dr. Maky Zanganeh and Associates, Inc.

On March 26, 2021, the Company entered into a sublease with Dr. Maky Zanganeh and Associates, Inc. ("MZA") consisting of 4,500 square feet of office space at 2882 Sand Hill Road, Menlo Park, CA (the "Sublease"). Dr. Maky Zanganeh is the sole owner of MZA. The sublease runs until September 2022. The rent payable under the terms of the sublease is equivalent to the proportionate share of the rent payable by MZA to the third-party landlord, based on the square footage of office space sublet by the Company, and no mark-up has been applied. During the year ended December 31, 2021, payments of $556, were made pursuant to the sublease.

April 20, 2021 Note Purchase Agreement

On April 20, 2021, subsequent to the repayment of the Initial Note, Mr. Robert W. Duggan entered into a second Note Purchase Agreement (the "Second Purchase Agreement") pursuant to which he loaned the Company $55,000 in exchange for the issuance by the Company of an unsecured promissory note (the "Second Note") in the amount of $55,000. The Second Note accrued interest at a rate per annum equal to 150% of the applicable 10 Year US Treasury rate, as adjusted monthly (initially estimated to be approximately 2.4%). The Company was permitted to prepay any portion of the second note at its option without penalty.

May 12, 2021 Rights Offering

On May 12, 2021, the Company closed its rights offering, which was fully subscribed. Aggregate gross proceeds from the rights offering of $75,000 from the sale of 14,312,976 shares of the Company's common stock, of which 11,365,921 shares were purchased by Mr. Robert W. Duggan and 389,977 shares were purchased by Dr. Maky Zanganeh, at price of $5.24 per share. In connection with the closing of the rights offering, the Second Note, issued by the Company in favor of Mr. Robert W. Duggan, matured and became due and was repaid using a portion of the proceeds from the rights offering.

21. Subsequent Event

On March 10, 2022, Mr. Robert W. Duggan, entered into a Note Purchase Agreement (the "2022 Note"), pursuant to which he has loaned the Company $25,000 in exchange for the issuance by the Company of an unsecured promissory note in the amount of $25,000. The 2022 Note is to accrue interest at a rate per annum equal to the prime rate as reported in the *Wall Street Journal*, which is 3.25% as of the effective date. The 2022 Note becomes due upon the earlier of (i) the consummation of a registered public offering with net proceeds of no less than $25,000 or (ii) 18 months from the date of issuance of the 2022 Note.

Exhibit 21.1

SUBSIDIARIES OF THE REGISTRANT

Name of Subsidiary	Jurisdiction of incorporation or organization
Summit (Oxford) Limited	England and Wales
Discuva Limited	England and Wales
Summit Therapeutics Sub Inc.	Delaware, USA
Summit Therapeutics Limited	England and Wales
Summit Corporation Limited	England and Wales
Summit (Wales) Limited	England and Wales
Summit (Cambridge) Limited	England and Wales
Summit Discovery 1 Limited	England and Wales
Summit Corporation Employee Benefit Trust Company Limited	England and Wales
MuOx Limited	England and Wales
Summit Infectious Diseases Limited	England and Wales

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-249316 and 333-251958) and Form S-8 (Nos. 333-249313 and 333-238582) of Summit Therapeutics Inc. of our report dated March 17, 2022 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, MA
March 17, 2022

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-249316 and 333-251958) and Form S-8 (Nos. 333-249313 and 333-238582) of Summit Therapeutics Inc. of our report dated March 31, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Reading, United Kingdom
March 17, 2022

Exhibit 31.1

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES
EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE
SARBANES-OXLEY ACT OF 2002**

I, Robert W. Duggan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Summit Therapeutics Inc. (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:
    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the Company's most recent fiscal quarter (the Company's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):
    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 17, 2022

By: /s/ Robert W. Duggan

Name: Robert W. Duggan

Title: Chief Executive Officer and Executive Chairman; Principal Executive Officer and Principal Financial Officer

Exhibit 32.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Summit Therapeutics Inc. (the "Company") for the year ended December 31, 2021, as filed with the U.S. Securities and Exchange Commission on the date hereof (the "Report"), the undersigned Robert W. Duggan, as Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his or her knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 17, 2022

By: /s/ Robert W. Duggan

Name: Robert W. Duggan

Title: Chief Executive Officer and Executive Chairman; Principal Executive Officer and Principal Financial Officer