

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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d)
of The Securities Exchange Act of 1934

February 22, 2023
Date of Report (Date of earliest event reported)

Ambrx Biopharma Inc.
(Exact name of registrant as specified in its charter)

Cayman Islands
**(State or other jurisdiction
of incorporation)**

001-40505
**(Commission
File Number)**

N/A
**(IRS Employer
Identification No.)**

10975 Torrey Pines Road
La Jolla, California
(Address of principal executive offices)

92037
(Zip Code)

(858) 875-2400
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, par value US \$0.0001 per share	N/A	The New York Stock Exchange *
American Depositary Shares, each representing seven ordinary shares, par value US \$0.0001 per share	AMAM	The New York Stock Exchange

* Not for trading, but only in connection with the listing of the American depositary shares on the New York Stock Exchange. The American depositary shares represent the right to receive the ordinary shares and are being registered under the Securities Act of 1933 pursuant to a separate Registration Statement on Form F-6. Accordingly, the American depositary shares are exempt from registration under Section 12(a) of the Securities Exchange Act of 1934 pursuant to Rule 12a-8 thereunder.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

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.

Item 5.02. Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On February 22, 2023, Edward Hu resigned from the board of directors (the “*Board*”) of Ambrx Biopharma Inc. (the “*Company*”), effective immediately. Mr. Hu’s decision to resign was not the result of any disagreement with the Company.

Item 7.01 Regulation FD Disclosure.

On February 24, 2023, the Company is hosting a conference call and webcast, where it will present a discussion of its candidates ARX788 and ARX517. A copy of the slide presentation to be presented during this event is attached to this Current Report on Form 8-K as Exhibit 99.1 and is incorporated herein by reference. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information provided in Item 7.01 of this Form 8-K, including Exhibit 99.1 hereto, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any of the Company’s filings under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On February 24, 2023, the Company announced that it plans to conduct a small signal-finding Phase 2 clinical trial of ARX788. The trial design will include approximately 30 patients with HER2+ metastatic breast cancer that have progressed following Enhertu® (trastuzumab deruxtecan). The Company plans to enroll patients that have had no more than three prior lines of therapy and have recent assessments of HER2+ status. The trial’s primary endpoint will be the overall response rate (investigator assessed). The Company estimates that enrollment will take approximately 18 months from the first patient dosed.

Forward-Looking Statements

This Current Report on Form 8-K includes certain “forward-looking statements” intended to qualify for the “safe harbor” from liability established by the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements may be identified by the words “could,” “estimate,” “plan,” “will,” and similar expressions, and include, without limitation, express or implied statements regarding the Company’s planned Phase 2 clinical trial of ARX788. Forward-looking statements are based on the Company’s current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, those risks and uncertainties associated with: risks and uncertainties associated with the Company’s business and finances in general; the Company’s ability to execute on its strategy including with respect to the timing of its research and development efforts, initiation of clinical trials and other anticipated milestones; risks associated with development of novel therapeutics, including potential delays in clinical trials and regulatory submissions and the fact that future clinical trial results may not be consistent with preliminary results or results from prior preclinical studies or clinical trials; the Company’s ability to fund operations as anticipated; risks associated with geopolitical and macroeconomic conditions, including the COVID-19 pandemic; and the additional risks and uncertainties set forth more fully under the caption “Risk Factors” in the Company’s Annual Report on Form 20-F filed with the United States Securities and Exchange Commission (the “SEC”) on April 26, 2022, and elsewhere in the Company’s filings and reports with the SEC. Forward-looking statements contained in this Current Report on Form 8-K are made as of this date, and the Company undertakes no duty to publicly update or revise any forward looking statements, whether as a result of new information, future events or otherwise, except as may be required under applicable law.

The information contained in this Current Report on Form 8-K is hereby incorporated by reference into the Company’s Registration Statement Form F-3 (Registration No. 333-266404).

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Analyst and Investor Day Presentation, dated February 24, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: February 24, 2023

AMBRX BIOPHARMA INC.

By: /s/ Sonja Nelson

Name: Sonja Nelson

Title: Chief Financial and Operating Officer

Analyst and Investor Day

February 24, 2023

The AMBRX logo is displayed in a large, sans-serif font. The letters 'A', 'M', and 'B' are colored in a gradient from yellow to green, while 'R', 'X', and the second 'M' are in a solid blue color. The background of the slide features a blue and green geometric pattern on the left and a cluster of blue and purple spheres on the right.

AMBRX

Forward-Looking Statements

Certain statements contained in this presentation, other than statements of historical fact, are "forward-looking" statements, within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by the use of words such as "believes," "expects," "hopes," "may," "will," "plan," "intends," "estimates," "could," "should," "would," "continue," "seeks," "pro forma," or "anticipates," or other similar words (including their use in the negative), or by discussions of future matters. These forward-looking statements include, without limitation, statements regarding the timing, progress and results of preclinical studies and clinical trials for our product candidates; our product development plans and strategies; plans and expectations with respect to regulatory filings and approvals; the potential benefits and market opportunity for our product candidates and technologies; expectations regarding future events under collaboration and licensing agreements, as well as our plans and strategies for entering into further collaboration and licensing agreements; expectations regarding our future financial position and results of operations; our expected cash runway; and expected benefits of our reprioritizing.

Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially and historical results should not be considered as an indication of future performance. These risks and uncertainties include, among others, risks inherent in the development and regulatory approval process for novel therapeutics; the fact that future preclinical and clinical results/data may not be consistent with initial or preliminary results/data or results/data from prior preclinical studies or clinical trials; potential delays in development timelines, including delays in clinical trials; the potential impact of the COVID-19 pandemic; our reliance on third parties for development and manufacturing activities; changes in competitive products or in the standard of care; the risk of early termination of collaboration agreements; the risk that our proprietary rights may be insufficient to protect our product candidates or that we could infringe the proprietary rights of others; the fact that we will need additional capital and such capital may not be available on acceptable terms or at all; and changes in laws and regulations. Other factors that may cause our actual results to differ from current expectations are discussed in our filings with the U.S. Securities and Exchange Commission, including the section titled "Risk Factors" contained therein.

Caution should be exercised when interpreting results from separate trials involving separate product candidates. There are differences in the clinical trial design, patient populations, follow-up times, and the product candidates themselves.

These forward-looking statements are based on information available to, and expectations of, Ambrx as of the date of this presentation. Ambrx disclaims any obligation to update these forward-looking statements, except as may be required by law. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

ARX788
Anti-HER2 ADC for
Patients with Post-Enhertu
HER2+ Metastatic Breast

AMBRX

Efficacy Signal Seen in Post-Enhertu Patients with ARX788

In October 2022, Ambrx strategically reprioritized its pipeline and paused further internal development of ARX-788, while seeking partnership

- ACE-Breast-03 study - Clinical study evaluating ARX788 in metastatic HER+ breast cancer (mBC) post-Enhertu and post-Kadcyla stopped enrollment of new patients
- ACE-Pan-Tumor-01 study - Clinical study evaluating ARX788 in multiple cancer types, including mBC; stopped enrollment of new patients
- Patients who were already enrolled continued to be treated and evaluated

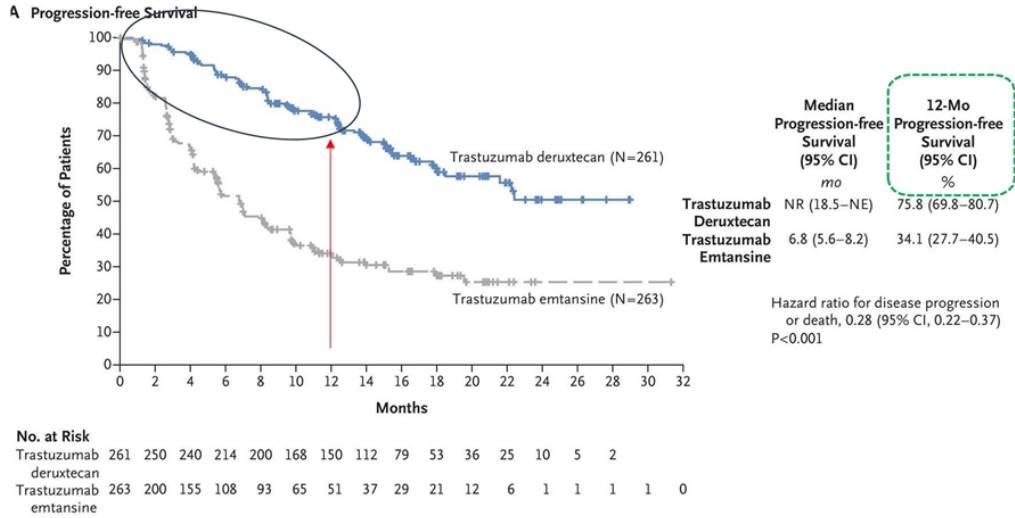
Preliminary data from these two studies shows anti-tumor activity in post-Enhertu, post-Kadcyla and HER2 low patients

- Data is in a small number of patients and some responses are unconfirmed
- Data anticipated to be presented at future medical meetings

Completed study (ACE-Breast-01) demonstrates robust response rate in the HER2 metastatic breast cancer (mBC) (next slide)

- Data published in Clinical Cancer Research (2022) and presented at San Antonio Breast Cancer Conference 2021

Enhertu changed the breast cancer ADC landscape, but 24.2% of patients on Enhertu progress within 12 months



No post-Enhertu data supporting the effectiveness of Kadcyla and/or Tukysa potentially creates a new large market opportunity with no standard of care

Post-Enhertu Market Could be a Billion Dollar Opportunity

Estimated Drug treated patients in 3L+ (ie, 3L or later) HER2+ BC: 10,000 to > 14,000, depending on source

- 9,800 drug-treated patients per DRG, March 2020 report; estimate for 2028, 7MM
- >14,000 patients per HER2 competitors Roche and AstraZeneca estimates of patient populations published in their investor materials (Sep, 2020 (Roche) and Jun, 2022 (AstraZeneca))

Assuming price is in line with Trodelvy (~\$25,000 for 4 wks) and similar PFS (~ 6 mo) equates to \$150,000 per patient per course

Assuming 50% lower pricing ex-US, this translates into a potential market opportunity greater than \$1B in annual peak sales

Further upside is possible if Enhertu is approved in 1L (ongoing Destiny-Breast 09 study), which may open opportunity for ARX788 in the 2L setting

Rationale for Continuing Evaluation of ARX788 in post-Enhertu mBC Patients

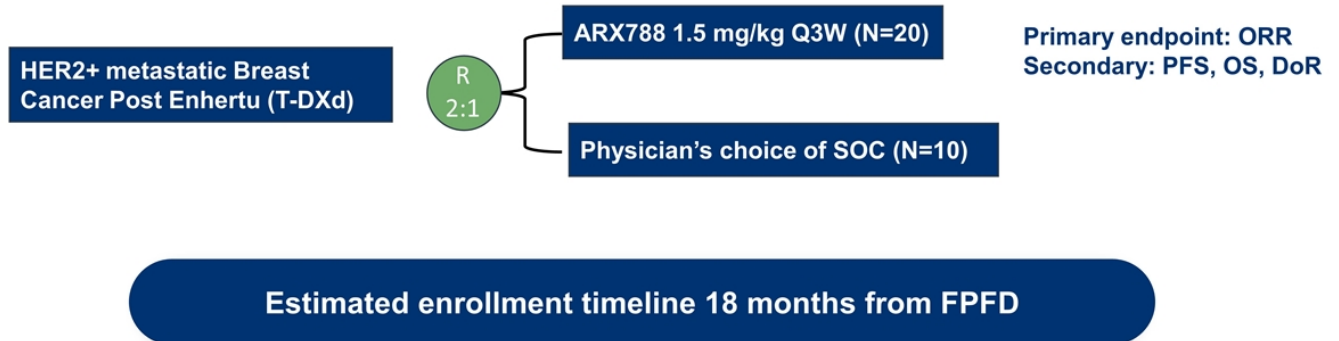
- Preliminary data from paused studies provide rationale for anti-tumor activity in post-Enhertu and post Kadcyła, as well as HER2 low patients
- Completed study (ACE-Breast-01) demonstrates robust response rate in the HER2 metastatic breast cancer (mBC)
 - Data published in Clinical Cancer Research (2022) and presented at San Antonio Breast Cancer Conference 2021
- ARX788 kills cancer cells with a different payload than Enhertu
 - Presentation at ESMO 22 from Mosele et al. assessing resistance to Enhertu concluded that: “Whereas HER2 expression decreased at progression on T-DXd, there is no robust evidence that T-DXd uptake reduction is the dominant mechanism of resistance” supporting the notion that a HER2-targeted ADC with a different payload should have efficacy
- High unmet medical need post Enhertu in HER2+ and HER2 low mBC
- Post-Enhertu market could be a multi-billion dollar opportunity
- Cost to evaluate ARX788 in post-Enhertu HER+ mBC patients outweighed by potential upside value creation

Planned Phase 2 Study of Approximately 30 Patients Post-Enhertu

Amend existing ACE-Breast-03 protocol and submit to FDA (approx. 3-month process)

- Leverage existing / open clinical trial sites in ACE-Breast-03 to enable quicker study start
- Patients with no more than 3 prior lines of therapy and recent assessment of HER2+ status
- Approximate study costs are \$20M - \$30M

If clinical signal of ~20-30% ORR, expand into a registration-enabled study



ARX517
Anti-PSMA ADC for Prostate
and Other Cancers

AMBRX

ARX517 - APEX-01 Phase 1 Trial Design

Objectives

Primary

- Safety
- Tolerability
- MTD
- RP2D

Secondary

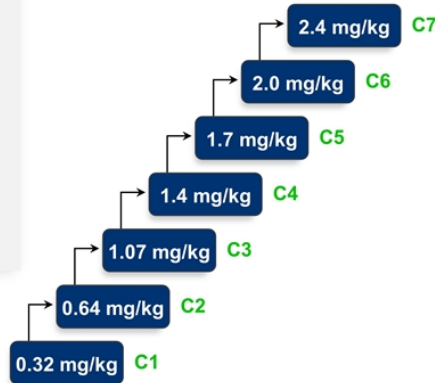
- Radiographic Response
- PSA Response (PSA30, PSA50, PSA90)

Dose Escalation

Q3W Dosing
i3+3 Design
(16-36 Patients)

MTD or RP2D
Expansion

Dose Expansion
in metastatic-castration
resistant prostate cancer
(mCRPC)
(Up to 40 Subjects)



- Promising early safety and efficacy signal observed
- No drug-related SAEs, no DLTs for all Cohorts evaluated (as of 2/16/23)
- In Cohort 6 (2.0 mg/kg dose), confirmed responses in the first 3 patients with a greater than 50% reduction in PSA levels, with two patients having a reduction in PSA >90%
- > 30% PSA reductions observed in one or more patients in all previous cohorts starting at 0.64 mg/kg
- Patients were heavily pretreated, with a median of five prior lines of therapy (including Pluvicto)

The Case for ARX517 in mCRPC

PSMA is highly expressed (89%) in metastatic castration resistant prostate cancer (mCRPC), as well as neovasculature of various solid tumors

PSMA is a clinically validated target and an established market for mCRPC

- Pluvicto has validated the PMSA as an effective prostate cancer target

Widespread adoption and clinical application of Pluvicto may be challenging due to the limitations on utilization caused by the radioligand¹

Because it is an infused product, and not a radioligand, we believe an opportunity exists for ARX517

- Referrals to radiation oncology / nuclear medicine may create burdens to patients due to the lower number of radiation oncology / nuclear medicine practitioners
- Medical oncologists would likely prefer to exhaust effective treatments that they can prescribe prior to referral to radiation oncology

¹ September 2022 market research

Appendix

AMBRX

ACE-Breast-01 (China) and ACE-PanTumor-01(US/AU)

ACE-Breast-01

- 69 patients were enrolled in China, ORR was 65.5%, the DCR was 100% and the median progression-free survival was 17.02 months.
- ARX788 was well tolerated with most adverse events being grade 1 or 2 and were manageable, low systemic toxicity was observed, no DLT or drug-related deaths occurred
- ARX788 has robust anti-tumor activity, generally good tolerance, circulating stability and unique pharmacokinetic profile in HER2-positive metastatic breast cancer patients who had progressed on prior anti-HER2 therapies.*

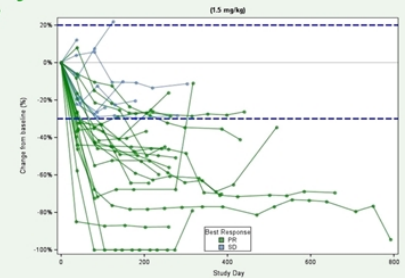
ACE-Pan Tumor-01

- ACE-Pan tumor-01 (US/AU) demonstrated comparable clinical response to ACE-Breast-01 with ORR at 67% and DCR 100% at 1.5mg/kg (N=3)

Confirmed ORR with ARX788 in patients whose disease is resistant or refractory to prior HER2 treatment (trastuzumab, ADCs, TKIs, and bispecific antibodies)*

Prior anti-HER2 therapy*	Confirmed ORR
Trastuzumab containing regimens*	19/29 (66%)
HER2 ADCs (T-DM1, DX126-262, A166, BAT8001, and HS630) regimens**	4/5 (80%)
HER2 TKIs (lapatinib, pyrotinib, neratinib, AST-1306, and Hemay-022) regimens	15/23 (65%)
Both HER2 ADC and HER2 TKI regimens	3/4 (75%)
Bispecific antibodies (KN026 and M802) containing regimens	3/4 (75%)

* All patients at 1.5 mg/kg Q3W received prior trastuzumab-containing regimens ** One patient who received prior pertuzumab also achieved confirmed PR.



*ACE-Breast-01 conducted in China by Ambrx's partner, NovoCodex Biologics
 Presented: San Antonio Breast Cancer Conference 2022
 Published: Clinical Cancer Research (2022) 28 (19): 4212-4221 (Zhang, et. al.) <https://doi.org/10.1158/1078-0432.CCR-22-0456>

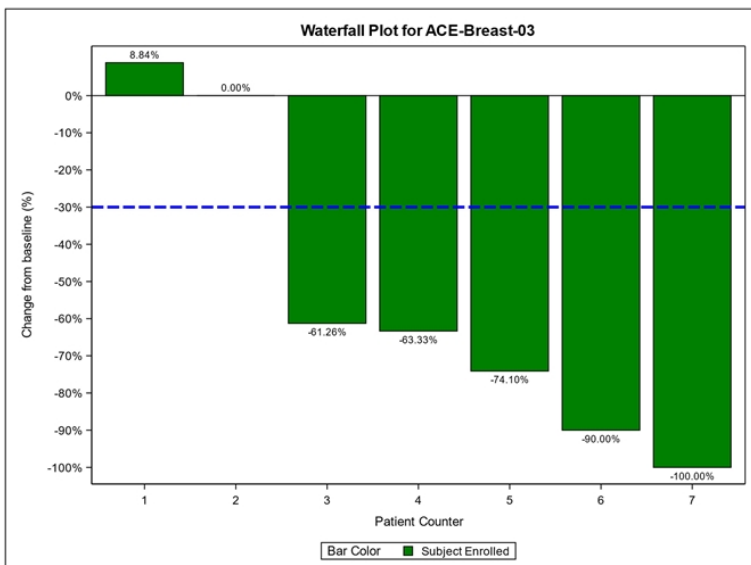
Data cut-off: June 30, 2021 **AMBRX**

Summary of ARX788 Safety Data (All Cohorts)

	ARX788 (All Treated Population) Number of patients (%)		
	ACE-Breast-01 (N=69)	ACE-Pan-Tumor- 01 (N=67)	ACE-Gastric-01 (N=30)
All AEs (regardless of causality)	69 (100%)	61 (91.0%)	29 (96.7%)
Drug-related AEs (any grade)	67 (97.1%)	48 (71.6%)	28 (93.3%)
All AEs ≥ Grade 3 and Grade 4 AEs	16 (23.2%)	23 (34.3%)	10 (33.3%)
Drug-related Grade 3 and Grade 4 AEs	8 (11.6%)	8 (11.9%)	4 (13.3%)
All SAEs	8 (11.6%)	17 (25.4%)	7 (23.3%)
Drug-related SAEs	2 (2.9%)	5 (7.5%)	2 (6.7%)
Drug-related AEs leading to discontinuation	3 (4.3%)	6 (9.0%)	2 (6.7%)
Drug-related Deaths	0	0	0

Data cut-off: Dec-14-2021 for ACE-Breast-01 (China), Dec-14-2021 for ACE-Gastric-01 (China), Dec-13-2021 for ACE-Pan-Tumor-01 (US/AUS)

ACE-Breast-03: ARX788 Provided a Clinical Benefit to Patient Previously Treated with Kadcylya (T-DM1)



Key Takeaways

- ARX788 provided clinical benefit to patients previously treated with T-DM1 who had disease progression
- 4/7 patients also previously received HER2 TKI treatment
- Confirmed objective response rate (ORR) was 57.1% (4/7 pts) and an unconfirmed ORR of 71.4% (5/7 pts)
- Disease control rate (DCR) was 100% (7/7 pts)
- Treatment with ARX788 remains ongoing with the median time of ARX788 therapy of 7.2 months
- ARX788 was well-tolerated, and AEs were manageable
- https://s27.q4cdn.com/912984828/files/doc_presentations/2022/12/2022-SABCS-ACE-Breast-03_Ambrx.pdf

San Antonio Breast Cancer Conference, 2022

Data from ACE-Breast-01 Demonstrates that ARX788 Has Competitive Activity in the HER2 ADC Landscape

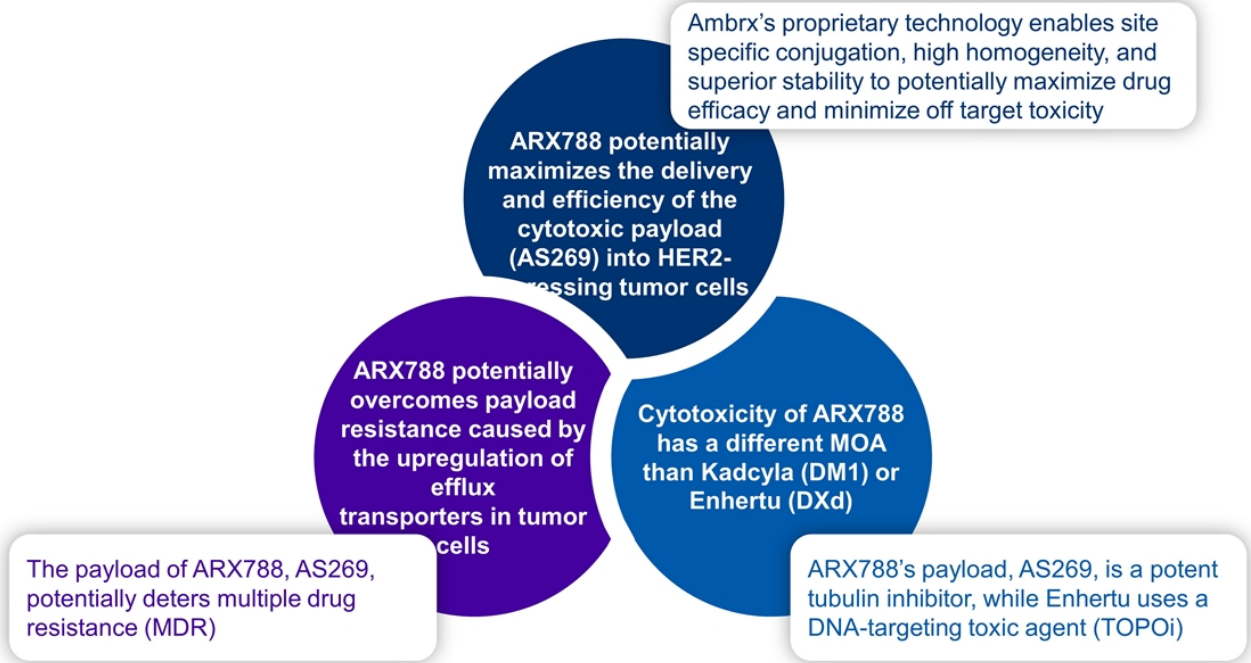
HER2 ADCs in Breast Cancer Efficacy Landscape

	Kadcyla (TDM1)	Enhertu (T-DXd)	Enhertu (T-DXd)	ARX788	RC48**	SYD985
Pop	2L	2L	3L	Median 5L	Median 4L	3L
ORR	35.0%	78.5%	69.7%	65.5%	41%	27.8%
DOR	23.8m	36.6m	19.6m	14.4m	-	
PFS	6.8m	28.8m	17.8m	17.0m	6m	7m
Source	DB03	DB03	DB04	ACE-Breast-01* Zhang	Wang	Saura

ARX788 has demonstrated robust ORR

FOR ILLUSTRATIVE PURPOSES ONLY – Not a head-to-head analysis
 *ACE-Breast-01 conducted in China by Ambrx's partner, NovoCodex Biologics
 **SeaGen acquired rights for RC48 for \$200M as well as \$2.4B in milestones

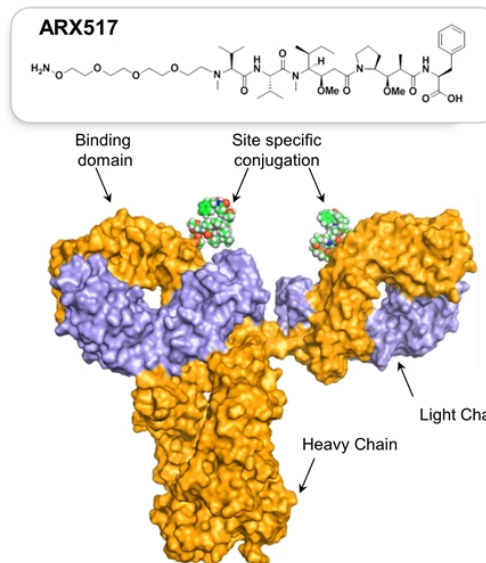
ARX788 Potential Mechanisms to Overcome Enhertu Resistance



ARX517 is the only ADC targeting PSMA in prostate cancer

- Fully humanized anti-PSMA monoclonal antibody (mAb) produced in CHO cells with site-specific incorporation of a SAA for conjugation
- Contains two (2) drug-linkers (AS269, a tubulin polymerization inhibitor) per mAb, a DAR 2 ADC
- Highly stable linkage – site-specific conjugation with via oxime chemistry

<https://clinicaltrials.gov/ct2/show/NCT04662580?term=arx517&draw=2&rank=1>



Potential to Become First-in-Class & Best-in-Class PSMA-ADC