zymeworks

Barclays Global Healthcare Conference

Kenneth Galbraith
Chair & CEO

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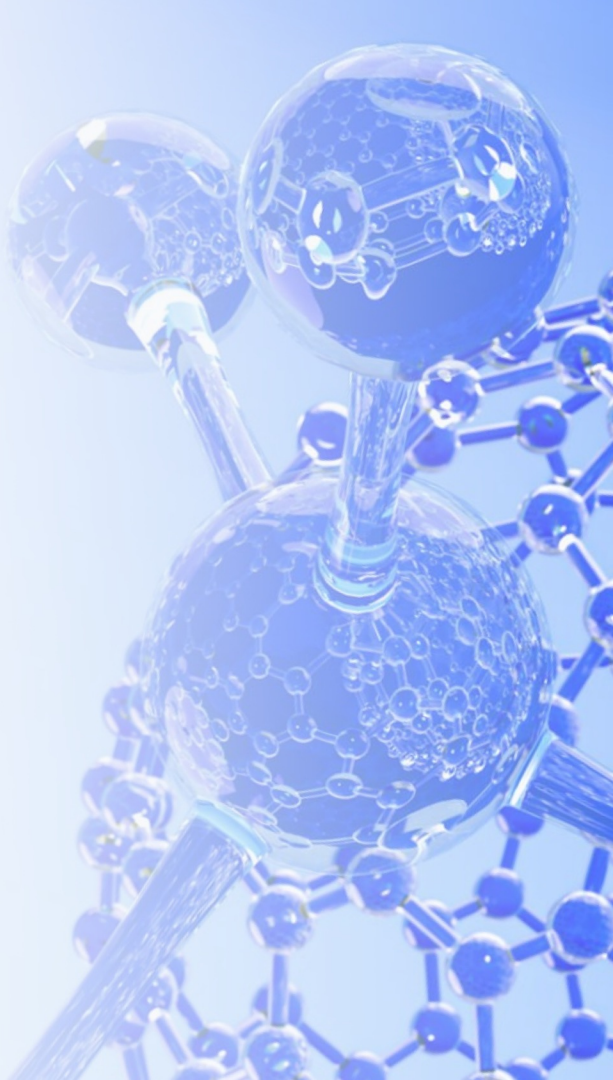

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These forward-looking statements are made only as of the date hereof, and Zymeworks Inc. undertakes no obligation to update or revise the forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Multifunctional Antibody Therapeutics for Oncology (and Beyond)

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Integrated R&D Engine

Multispecific Antibody Therapeutics (MSAT)

Antibody Drug Conjugates (ADC)

Focus on indications with worst patient prognosis (e.g., 5-year OS)

Product Profile

First and Second-line

market opportunities

Accelerated Approval

regulatory pathway allows potential of early market entry

Pursue lead indications with global peak sales potential >$500MM per product

Enterprise Value Framework

Our Strategy

Zymeworks is well-positioned to build upon our key priorities and enhance shareholder value through focusing on our Enterprise Value Framework

Enterprise value framework focuses on delivering progress across all five key elements through 2023 and 2024

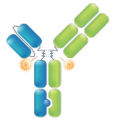
Goal of optimizing value as measured by per share returns for shareholders over the long-term

Jazz Pharmaceuticals

Global[1] Zanidatamab Collaboration with Jazz Pharmaceuticals

BeiGene

Zanidatamab Collaboration with BeiGene in APAC



Zanidatamab Zovodotin

Research and Early Development Programs

Legacy Technology Licensing Portfolio

APAC: Asia-pacific region

[1] Under the terms of the agreement, Jazz received an exclusive license to develop and commercialize zanidatamab in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories that Zymeworks previously licensed to BeiGene, Ltd

Key Priorities for 2023 and 2024

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1 Financial Transformation

Transformation of financial position **ensures funding of key priorities** for multiple years and ability to opportunistically fund R&D engine

2 Purposeful Development

Further **evaluate zanidatamab zovodotin in key indications**, as monotherapy and in combination, to provide potential rationale for future registrational studies

3 Drive Value

Continue to **aggressively pursue** and **drive value** through partnerships and collaborations

4 Collaborate

Maximize value of zanidatamab brand through support of key commercialization partners, Jazz and BeiGene

KEY PRIORITIES	STATUS/TARGET
Zanidatamab Commercialization Support	
Continue to report additional zanidatamab data	1H23
Update on development pathway in key indications	Ongoing
Updated timing on requisite regulatory filings	Ongoing
Research and Early Development Programs	
Submit IND for two lead preclinical programs (ZW171 / ZW191)	2024
Nominate additional preclinical product candidate for 2025 IND	2023
Continue actively presenting and publishing preclinical data	April - AACR
Aggressively pursue collaboration and partnerships	Ongoing
Zanidatamab Zovodotin	
Present additional data from Ph1 clinical study	2023
Initiate multiple Ph 2 clinical studies – NSCLC & mBC	2023
Legacy Platform Licensing Portfolio	
Earn additional milestone payments from existing agreements	Ongoing
Evaluate potential for monetization or expansion	Ongoing

AACR: American Association of Cancer Research; IND: investigational new drug application; mBC: metastatic breast cancer; NSCLC: non-small cell lung cancer; R&D: research and development; RP2D: Recommended Phase 2 dose

Novel Platforms Enable Unique and Differentiated Product Portfolio

Platforms Driving the Next Generation of Antibody Based Therapeutics

Azymetric™

Multispecific Antibody Generation

- Biparatopic/Bispecifics
- Trivalent/Trispecifics
- T-cell engager technology
- Fc-Fusions
- IgG1-like biophysical, manufacturing, and purification protocols

Drug Conjugate Platforms

Fit-For Purpose ADC Candidate Creation

- ZymeLink™ Auristatin
- ZymeLink™ Hemiasterlin
- TOPO1i Technology
- Cysteine-Insertion Conjugation Technology
- Immune Stimulating (TLR7)

EFECT™

Tailored Immune Function Modulation

- Tailored sets of Fc modifications that can modulate immune cell recruitment and function
- Enhance or eliminate immune effector function to optimize therapeutics

ProTECT™

Tumor-Specific Immune Co-stimulation

- Tumor-specific activity via conditional blocking to reduce off-tumor toxicities
- Functional block adds co-stimulation or checkpoint modulation to enhance efficacy

Enable New Biology | Modular | Scalable

Zymeworks Technology Platforms Proven to Generate Differentiated and Clinically-Validated Therapeutics

Multispecific

Zanidatamab (ZW25)

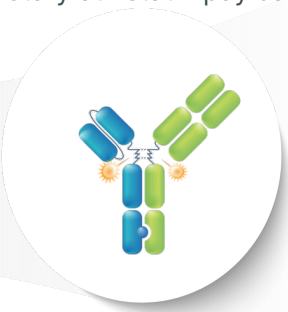
Biparatopic anti-HER2

Unique biology lends additional benefit achieved by mAb combinations

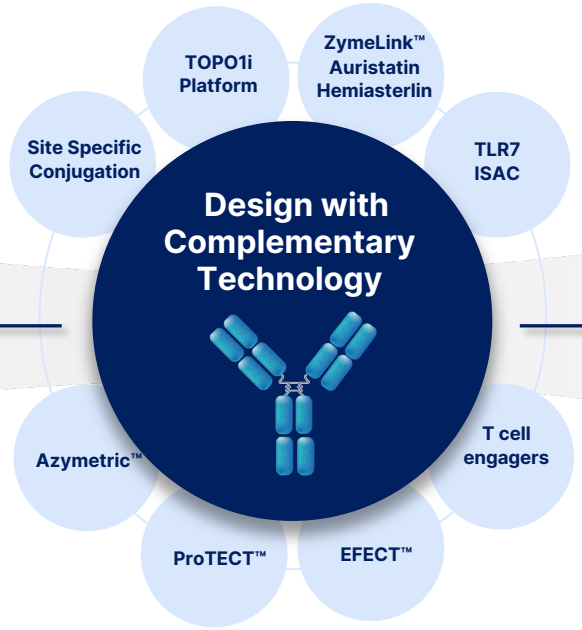
Antibody Drug Conjugate

Zanidatamab Zovodotin (ZW49)

Biparatopic anti-HER2 with proprietary auriastatin payload



Efficient internalizer and payload delivery



Pivotal clinical studies

Goal of 5 **New** INDs in 5 years

Clinical POC study

DAR: drug to antibody ration; Fc: fragment crystallizable region of antibody; HER2: human epidermal growth factor receptor 2; IND: investigational new drug application; ISAC: Immunostimulatory Drug Conjugate; MOA: mechanism of action; POC: proof of concept

A Growing Product Candidate Pipeline of Potential Best-in-Class Therapeutics

Zanidatamab	Preclinical	Phase 1	Phase 2	Pivotal	Collaboration Partner
1st-Line Gastroesophageal Adenocarcinomas HERIZON-GEA-01 Chemotherapy Combination					BeiGene Jazz Pharmaceuticals
2nd-Line Biliary Tract Cancers HERIZON-BTC-01 Monotherapy					BeiGene Jazz Pharmaceuticals
1st-Line Gastrointestinal Cancers Gastroesophageal Adenocarcinoma, Biliary Tract Cancer, and Colorectal Cancer Chemotherapy Combination					BeiGene Jazz Pharmaceuticals
Zanidatamab Monotherapy & Chemotherapy Combination					BeiGene Jazz Pharmaceuticals

A Growing Product Candidate Pipeline of Potential Best-in-Class Therapeutics

Early Development and Early R&D	Preclinical	Phase 1	Phase 2	Pivotal	Partner
Zanidatamab Zovodotin[1] HER2-Expressing Cancers Indications: NSCLC, mBC					BeiGene
ZW191 Folate Receptor-α Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: OVCA, Gynecological, NSCLC, TNBC					
ZW171 2+1 MSLN x CD3 Bispecific Antibody Indications: Pancreatic, OVCA, CRC					
ZW251 Glypican-3 Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: Hepatocellular carcinoma					
ZW220 NaPi2b Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indication: OVCA, NSCLC, other solid tumors					

[1] Phase 2 studies to be initiated in 2023

BC: breast cancer; CRC: Colorectal cancer; GEA: gastroesophageal adenocarcinoma; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer; TNBC: triple negative breast cancer

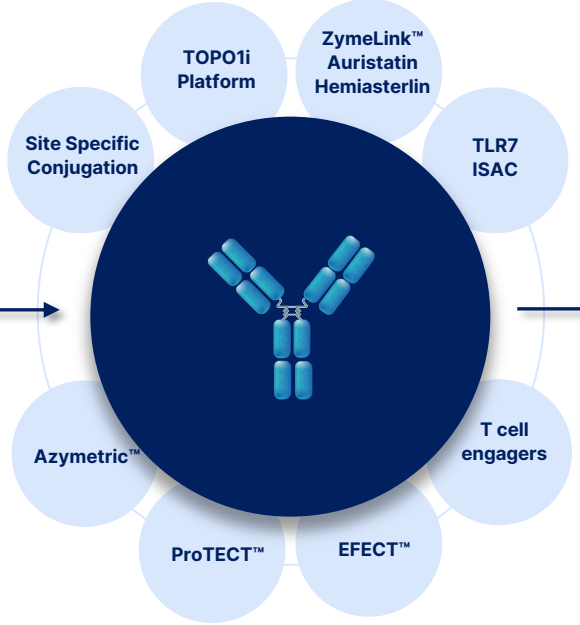
RESEARCH & DEVELOPMENT

Platforms and Product Candidates

ADC and Multispecific Modalities Driving Our Pipeline

Select Difficult-to-Treat Cancers & Target

Design with Complementary Technology

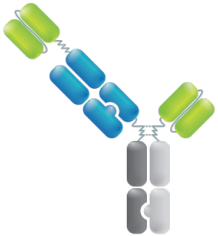


Optionality with Two Foundational Fit-for-Purpose Modalities

Anti-body Drug Conjugates

Customization:

- Antibody properties
- Antibody format
- Payload
- DAR



Multi-specifics

Customization:

- Multiple MOA in single molecule
- Synergistic biology
- Precision targeting through multivalency

DAR: drug to antibody ration; MOA: mechanism of action

Zymeworks Multispecific T Cell Engager Strategy: Utilizing Azymetric™ to Build Differentiated & Next Generation Multispecific T Cell Engagers

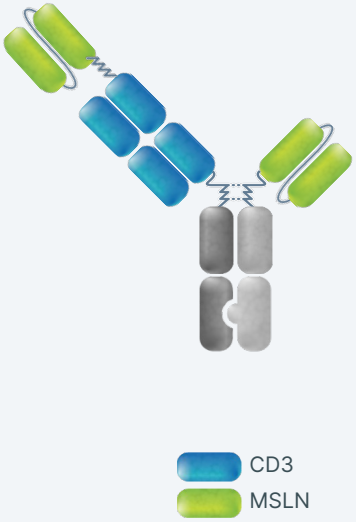
Biological Problem	Zymeworks Solution
1 Narrow therapeutic window and toxicity due to CRS associated with Gen 1 TCE in solid tumors	**2+1 T Cell Engager (ZW171)** Mitigate cytokine release syndrome with low affinity T cell binding and enhanced efficacy and selectivity with avidity-driven tumor antigen binding
2 Limited T cell intratumoral availability and T cell anergy in solid tumors	**TriTCE Co-stimulation** Increase T cell fitness, activation and proliferation via tumor-dependent T cell co-stimulation
3 Immunosuppressive tumor microenvironment limiting T cell responses in solid tumors	**TriTCE Checkpoint Inhibitor** Increase T cell responses through simultaneous checkpoint blockade and avidity-driven binding

TCE: t cell engager

ZW171: 2+1 Bispecific MSLN x CD3 T Cell Engaging Antibody

Lead Preclinical Product Candidate

ZW171



MSLN Targeted

Antibody targets mesothelin (MSLN), a glycoprotein that is elevated in many cancers including pancreatic, mesothelioma and ovarian cancer

Target is clinically validated, indications have high unmet clinical need

CD3 Targeted

Targeting CD3 receptor to redirect T cell cytotoxicity towards cancerous cells

Anti-CD3 antibody targeting novel epitope that mediates low T cell binding and cytokine release and potent tumor cell lysis

Format Engineering

Extensive assessment of different formats with different valences & geometries

2+1 dual scFv identified as avidity-driven format with optimal activity and safety profile

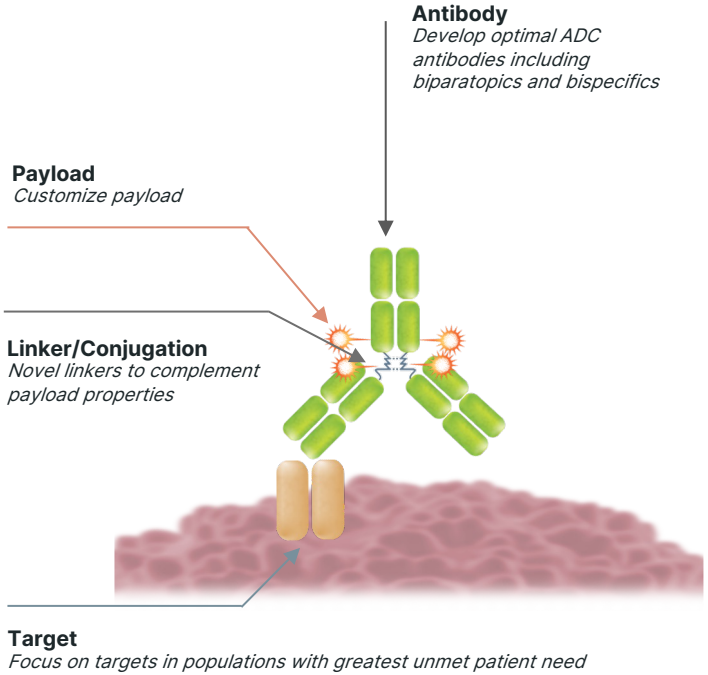
Validation

In preclinical development

Targeting IND 2024

Designing Fit-for-Purpose ADC Candidates

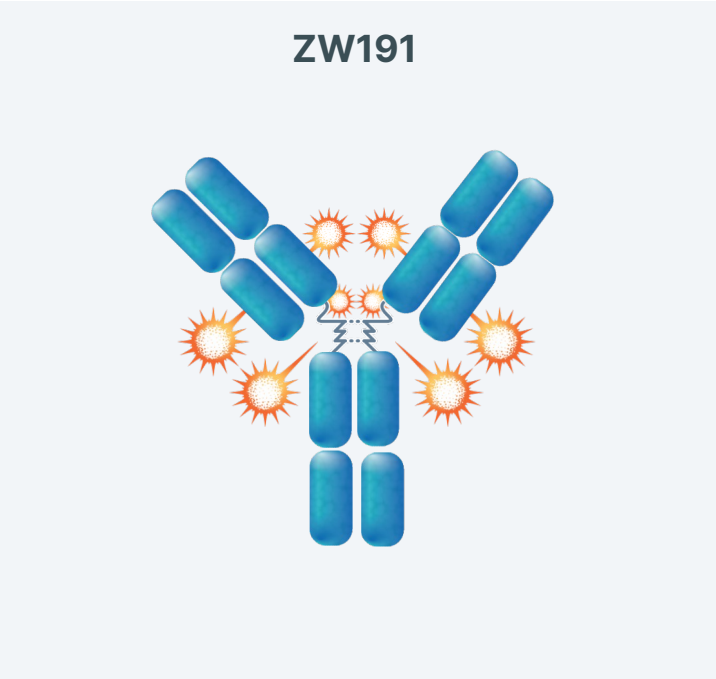
	Zymeworks Strategy Today	Zymeworks Strategy Tomorrow
Target	Focus on targets with evidence of clinical activity in indications of unmet need	Explore novel targets
Antibody	Develop optimal ADC antibodies	Leverage bispecific and biparatopic expertise to develop optimal ADC antibodies
Linker/ Conjugation	Leverage validated peptide-cleavable linkers & stochastic conjugation	Design novel linkers to complement payload properties
Payload	Focus on novel TOPO1i ADC technology	Develop novel payloads by adapting MoAs with clinical validation to novel ADC application



ADC: antibody drug conjugate; MOA: mechanism of action; TOPO1i: topoisomerase inhibitor

ZW191: Folate Receptor Alpha Topoisomerase-1 Inhibitor ADC

Lead Preclinical Product Candidate



Target

Folate receptor alpha (FRα, FOLR1) is a clinically validated ADC target

FRα is over-expressed on the cell surface of ovarian cancer, other gynecological cancers, and additional high incidence solid tumors with unmet medical need (NSCLC, TNBC, etc.)

Antibody

Internally discovered, novel IgG1 monospecific antibody

Optimal internalization, payload delivery and tumor penetration

Drug Linker

Cysteine conjugated, DAR8, protease cleavable, traceless drug-linker

Novel bystander-active topoisomerase-1 inhibitor

Status

MTD ≥ 30 mg/kg in two dose non-human primate (NHP) toxicology study, with favorable PK

Strong anti-tumor activity in models with a range of expression

Targeting 2024 IND

ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio; NSCLC: non small cell lung cancer; MTD: maximum tolerable dose; TNBC: triple negative breast cancer

Zymeworks Moving Forward “5 by 5”

5 new product candidates planned for IND's over next 5 years

2017-2022

- Select Product Pipeline
- Platform Technologies & Tools

2022-2027

- **Accelerate Product Pipeline**
- **5 New Molecules in Clinic in 5 Years**
- **Select Product Partnerships**

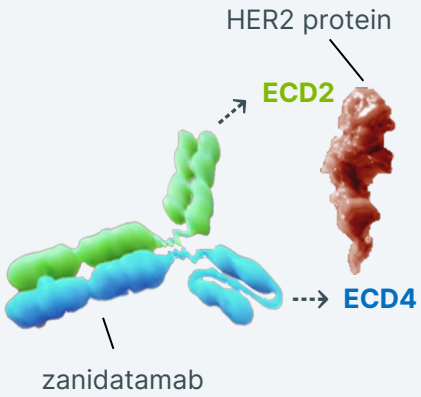
ZANIDATAMAB

Commercial Collaborations

Transactions allow zanidatamab reach a broad group of patients globally and may improve patient outcomes beyond the current standards of care, pending regulatory approval

Zanidatamab: A Bispecific Antibody for HER2-Expressing Cancers

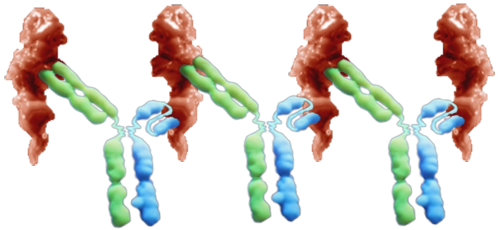
Zanidatamab



Zanidatamab's Unique Binding Geometry Promotes:

- Biparatopic – targets two distinct HER2 epitopes and results in HER2 binding across a range of expression levels (low to high)
- HER2-receptor cross-linking, clustering, internalization, and downregulation
  - Enhanced receptor clustering on cell surface (cluster internalization, receptor downregulation)
  - Inhibition of cellular proliferation
- Fc-mediated cytotoxicity: ADCC, ADCP, CDC

Dual HER2-Binding of Zanidatamab Drives Unique MOA



The geometry of zanidatamab prevents it from binding to the same HER2 molecule

Note: Zanidatamab has been granted Breakthrough Therapy designation by the FDA for patients with previously-treated HER2 gene-amplified BTC as well as two Fast Track designations, one for previously treated or recurrent HER2-positive BTC and another for first-line GEA in combination with standard of care chemotherapy. Zanidatamab also received Orphan Drug designation for the treatment of BTC and GEA in the United States and for gastric cancer and BTC in the European Union.
ADCC: antibody-dependent cellular cytotoxicity; ADCP: antibody-dependent cellular phagocytosis; CDC: complement-dependent cytotoxicity; ECD: extracellular domain; Fc: fragment crystallizable region of antibody; HER2: human epidermal growth factor receptor 2

Key Financial Terms of Licensing Agreement with Jazz

	Licensing Agreement Terms[1]
Counterparty	Jazz Pharmaceuticals
Upfront Payments	$375,000,000 received in 4Q22
Regulatory Milestones	Up to $525,000,000
Commercial Milestones	Up to $862,500,000
Royalties	Tiered royalties of 10 to 20% of net sales
Current R&D Spend	All costs for ongoing clinical studies to be reimbursed 100% by Jazz[2]
Territories	US, EU, Japan and all other territories except those in Asia Pacific not covered by BeiGene agreement
Future R&D Spend	Jazz to fund 100% of costs of future studies

Key Benefits to Zanidatamab Licensing Agreement:

- **Meaningful improvement to financial position and reduction in future expenditures** allows focus on growth of exciting early-stage pipeline while zanidatamab advances to commercialization
- **Accelerate** and **expand R&D programs** (early R&D and ZW49) while maintaining anticipated cash runway through at least 2026 with a goal of advancing ***5 new programs into clinical studies in 5 years***
- **Continued management** of existing zanidatamab program by Zymeworks, in partnership with Jazz, including first BLA, **leveraging existing internal expertise to progress programs rapidly**, with future zanidatamab-related clinical studies, regulatory filings, and commercialization to be managed and funded by Jazz
- **Substantial potential milestone payments** based on global regulatory milestones for zanidatamab in BTC and GEA with further upside from royalties and commercial milestones
- **Leverage** Jazz's global commercial infrastructure together with BeiGene's complementary strengths in APAC regions to **optimize commercialization of zanidatamab without requirement for investment in commercial infrastructure** within Zymeworks

[1] All dollar values in US Dollars
[2] Costs related to ongoing clinical studies incurred after signing of the agreement to be reimbursed 100% by Jazz, includes approximately $24M in reimbursable amounts from 4Q22

Key Financial Terms of Asia Pacific Licensing Agreement with BeiGene

	Licensing Agreement Terms[1]
Counterparty	BeiGene
Upfront Payments	$40,000,000
Development and Commercial Milestones	Up to $390,000,000
Royalties	Tiered royalties of up to 20% of net sales in BeiGene territories
Territories	Asia-Pacific region (excluding Japan and India)
Co-development Funding	Currently for BTC and GEA global development

Additional Details:

- Received $40MM upfront payment in 2018 and $20MM in milestones to-date
- BeiGene has development and commercial rights to zanidatamab and zanidatamab zovodotin
- Collaborate on certain global studies including HERIZON-BTC-01 and HERIZON-GEA-01 with BeiGene responsible for clinical and regulatory activities in their territory
- Co-development funding agreed for any global studies

[1] All dollar values in US Dollars

Advancing Pivotal Studies in BTC and GEA

HERIZON-BTC-01
A Global Pivotal Study in Second-Line HER2-Amplified BTC

Population: PATIENTS WITH HER2-AMPLIFIED BTC WHO RECEIVED PRIOR GEMCITABINE
N = 100
Cohort 1: 75 with IHC 2+ or 3+
Cohort 2: 25 with IHC 0 or 1+

Regimen: 28 Day Cycles
Day 1: Zanidatamab, 20 mg/kg IV
Day 15: Zanidatamab, 20 mg/kg IV
Every 8 Weeks CT/MRI

Locations: Canada, USA, Chile, France, Italy, Spain, United Kingdom, China, South Korea

Primary End Points: ORR

Secondary End Points: Proportion of patients with DOR ≥16 weeks, DOR, DCR, PFS, OS, safety

Additional Details: topline data presented late 2022 with full data readout anticipated in 1H23

HERIZON-GEA-01
A Global Pivotal Study in First-Line HER2-Positive GEA

Population: PATIENTS WITH HER2-POSITIVE ADVANCED OR METASTATIC GEA
N = 714

Regimen: 21 Day Cycles
ARM 1: Trastuzumab + SOC chemotherapy, N=238
ARM 2: Zanidatamab + SOC chemotherapy, N=238
ARM 3: Zanidatamab + tislelizumab + SOC chemotherapy, N=238
Assessment Every 6 weeks for first 54 weeks, Every 9 weeks thereafter

Locations: Australia, China, India, Malaysia, South Korea, Singapore, Taiwan, Thailand, Belgium, Czech Republic, Estonia, France, Italy, Georgia, Germany, Greece, Ireland, Netherlands, Poland, Portugal, Romania, Serbia, South Africa, Spain, Turkey, Ukraine and United Kingdom, Canada, Mexico, Guatemala, Argentina, Brazil, Chile
Peru

Primary End Points: PFS, OS

Secondary End Points: ORR, Frequency and Severity of AEs, Change in HRQOL from baseline

Additional Details: anticipate full data readout in 2024

[a] SOC (standard of care) chemotherapy: CAPOX or FP; [b] response assessments until progression per BICR or withdrawal of consent BICR: Blind independent central review; GEA: gastroesophageal adenocarcinoma; PFS: Progression-free survival; OS: overall survival

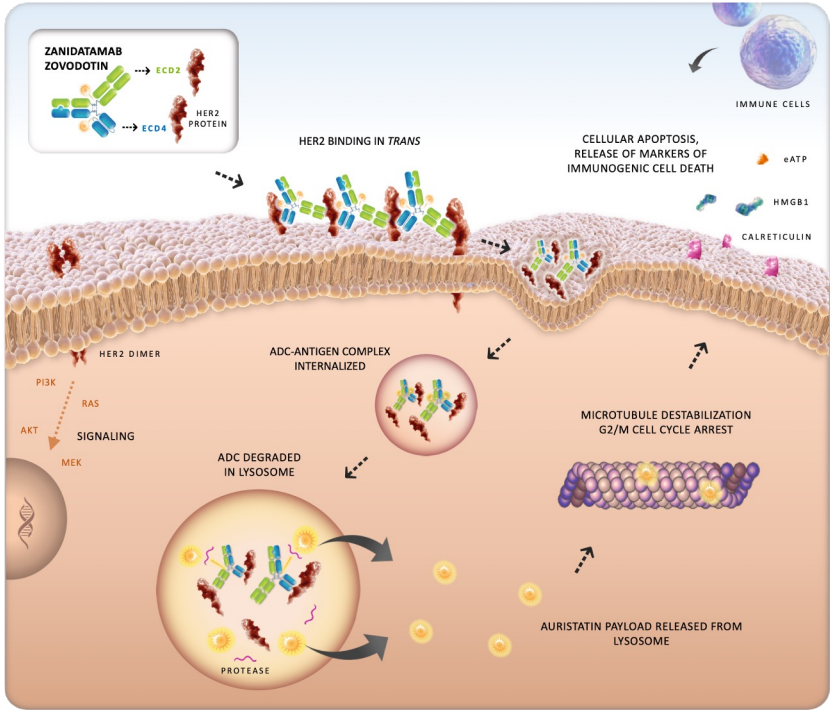
ZANIDATAMAB ZOVODOTIN

Clinical Development

Zanidatamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy

Unique Mechanism of Action[1,2,3]

- IgG1-like biparatopic antibody backbone directed against ECD4 & ECD2 of HER2
- Antibody sequence identical to zanidatamab
- Proprietary auristatin payload covalently linked to the antibody via a protease-cleavable linker
- Average drug-to-antibody ratio (DAR) of 2
- Biparatopic antibody-induced internalization with increased auristatin-mediated cytotoxicity and immunogenic cell death
- Potential to address unmet need in cancers with high and low levels of HER2 expression and HER2 mutations



ADC, antibody-drug conjugate; AKT, serine-threonine protein kinase family; eATP, extracellular adenosine 5'-triphosphate; ECD, extracellular domain; HER, human epidermal growth factor receptor; HMGB1, high mobility group box 1; G2/M, second gap phase/mitotic phase; MEK, mitogen-activated protein kinase kinase; PI3K, phosphatidylinositol 3-kinase; RAS, rat sarcoma pathway

1. Hamblett et al., #3914 Poster Presentation at AACR 2018; 2. Davies et al., #3912, Poster Presentation at AACR 2018; 3. Data on file

Zanidatamab Zovodotin: Focused and Strategic Development Path

Zanidatamab zovodotin

has shown single-agent activity in multiple tumor types with a differentiated tolerability profile amongst other HER2-targeted ADCs and has multiple pathways for development

Planned Phase 2 Studies

Non-Small Cell Lung Cancer (NSCLC)

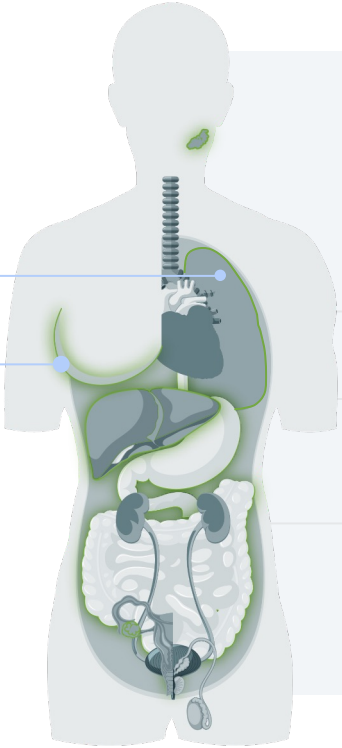
HER2-targeted NSCLC

Metastatic Breast Cancer (mBC)

HER2-positive mBC after progression with T-DXd
HER2-low mBC

Path Forward

- Phase 1 dose escalation to continue in Japan
- Present additional Phase 1 data in 2023
- Initiate separate Phase 2 clinical studies, expect study start in 2023
- Confirm ex-US partnership prior to start of registrational pathway by end of 2025



DIFFERENTIATED STRATEGY

Differentiated tolerability profile with no interstitial lung disease, no significant neuropathy, and no significant neutropenia noted to date

Single-agent activity across multiple HER2-expressing tumor types

Strategy to combine with standards of care across indications, with no known overlapping toxicities

Incrementally staged investment in clinical development to **preserve and maintain** cash runway

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

Zanidatamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy

Data Highlights and Catalysts

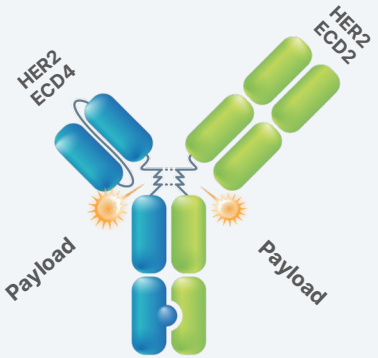
Clinical Data Highlights

- Differentiated tolerability profile amongst HER2-targeted ADCs with the majority of adverse events being grade 1 or 2 and manageable
- Confirmed ORR of 31%, disease control rate of 72% observed across 29 response-evaluable patients treated with zanidatamab zovodotin at 2.5 mg/kg Q3W
- Clear single-agent activity in heavily pretreated patients with potential go-forward regimen of 2.5 mg/kg dosed every three weeks

Expected Catalysts

- Update on progression of weekly expansion and escalation cohorts in 2023
- Expansion of Phase 2 to begin 2023
- Expect to commence enrollment before the end of 2023

Zanidatamab zovodotin



Unique mechanism of action, tolerability profile, and clear single-agent activity support measured and incremental future development strategy

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022; ORR: objective response rate

Legacy Technology License Portfolio

Legacy Partnerships & Collaborations Validate Zymeworks' Technology

Programs & Platforms	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
Bispecific Antibody Azymetric | EFECT	Oncology				Bristol Myers Squibb[1]
XB002 (ICON-2) Tissue Factor ADC ZymeLink	Solid Tumors				EXELIXIS[2]
JNJ-78278343 CD3 x KLK2 Bispecific Azymetric | EFECT	Castration-Resistant Prostate Cancer				Johnson & Johnson Innovation
Antibody Drug Conjugate ZymeLink	Oncology				ATRECA
Bispecific Antibody Azymetric | EFECT	Undisclosed				MERCK
Bispecific Antibody Azymetric | EFECT	Immuno-Oncology				Daiichi-Sankyo
Bispecific Antibody Azymetric | EFECT	Infectious Disease/Undisclosed				gsk
Bispecific Antibody Azymetric | EFECT	Dermatology				LEO
Bispecific Antibody Azymetric | EFECT	Undisclosed				BeiGene

Approximately $180MM[3] in milestones received to-date

[1]Original Agreement with Celgene (which is now a Bristol-Myers Squibb company)
[2]Original Agreement with Iconic; XB002 in-licensed by Exelixis
[3] Excludes Upfront Payments and milestones received in association with zanidatamab partnerships

Thank You