Zanidatamab License and Collaboration Agreement Webcast

October 19th, 2022

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NYSE: ZYME

www.zymeworks.com

Forward-Looking Statements

This presentation includes “forward-looking statements” or information within the meaning of applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this presentation and the accompanying oral statements include, but are not limited to, statements that relate to Zymeworks’ expectations regarding implementation of its corporate goals and meeting expected timelines; Zymeworks’ clinical development of its product candidates; related clinical trials; anticipated clinical data presentations and the timing thereof; potential therapeutic effects of zanidatamab and its other product candidates; expected financial performance and future financial position; the commercial potential of technology platforms and product candidates; anticipated continued receipt of revenue from existing and future partners; Zymeworks’ preclinical and early stage pipeline and the advancement of such pipeline; anticipated sufficiency of cash resources and other potential sources of cash to fund Zymeworks’ planned operations; Zymeworks’ ability to execute new collaborations and partnerships; advancement of zanidatamab zovodotin into registrational studies and other product candidates in clinical studies; Zymeworks’ ability to satisfy potential regulatory and commercial milestones with existing and future partners; anticipated benefits of our agreement with Jazz Pharmaceuticals; our anticipated cash runway following closing of the agreement with Jazz Pharmaceuticals; the commercial potential of zanidatamab and our and Jazz Pharmaceuticals’ ability to obtain regulatory approval of and successfully commercialize zanidatamab; the anticipated timing of closing of our agreement with Jazz Pharmaceuticals and satisfaction of closing conditions; the timing and status of ongoing and future studies and the related data; the timing of and results of interactions with regulators; and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “future,” “potential,” “progress,” “subject to,” “anticipate,” “plan,” “expect,” “estimate,” “project,” “may,” “will,” “could,” “can,” “advance”, the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements, including, without limitation, Zymeworks’ examination of historical operating trends, are based upon our current expectations and various assumptions. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: clinical trials may not demonstrate safety and efficacy of any of Zymeworks’ or its collaborators’ product candidates; any of Zymeworks’ or its partners’ product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; Zymeworks’ assumptions regarding its financial condition or future financial performance may be incorrect; Zymeworks may not be able to maintain or enter into new partnerships or strategic collaborations; Zymeworks may not be able to achieve additional milestones and receive related payments and royalties from existing or future collaborations; Zymeworks may not be able to obtain clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 and satisfy the other terms and conditions of the transactions contemplated by the License and Collaboration Agreement between Zymeworks and Jazz Pharmaceuticals; the impact of the COVID-19 pandemic on Zymeworks’ business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks’ behalf, may be more severe and more prolonged than currently anticipated; and the factors described under "Risk Factors" in Zymeworks’ quarterly and annual reports and other sections of our public filings with the Securities and Exchange Commission and Canadian securities regulators.

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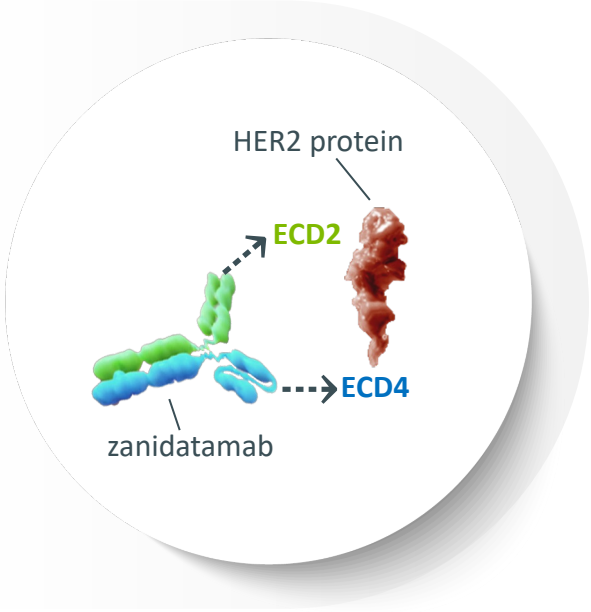
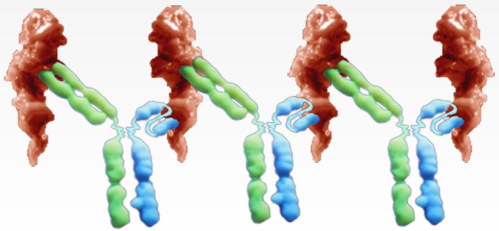
Zanidatamab: A Bispecific Antibody for HER2-Expressing Cancers



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

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Zanidatamab: Developed Internally with ZYME Protein Engineering Expertise

2013 - 2014

- First biparatopic anti-HER2 antibody expressed
- Cell-line development started

2016

- IND accepted by FDA
- First patient dosed in Phase 1 clinical trial

2018

- First clinical data presented at ASCO
- Zymeworks and BeiGene announced license and collaboration agreement for zanidatamab in APAC region

2019

- Initiated first Phase 2 clinical trial in 1L GEA
- Zanidatamab granted Fast Track and Orphan Drug designation by FDA

2020

- Initiated pivotal trial in advanced HER2-amplified BTC
- Zanidatamab receives Breakthrough Therapy Designation in BTC
- Phase 1 data in GEA presented at ASCO GI

2021

- Initiated global Phase 3 pivotal in 1L GEA

2022

Announces Global Licensing Agreement[1] with Jazz Pharmaceuticals

APAC: Asia Pacific; ASCO: American Society of Clinical Oncology Annual Meeting; BTC: Biliary Tract Cancer; FDA: US Food and Drug Administration; GEA: gastroesophageal adenocarcinoma; IND: investigational new drug application

[1] Excludes commercial territories in Asia Pacific countries controlled by BeiGene

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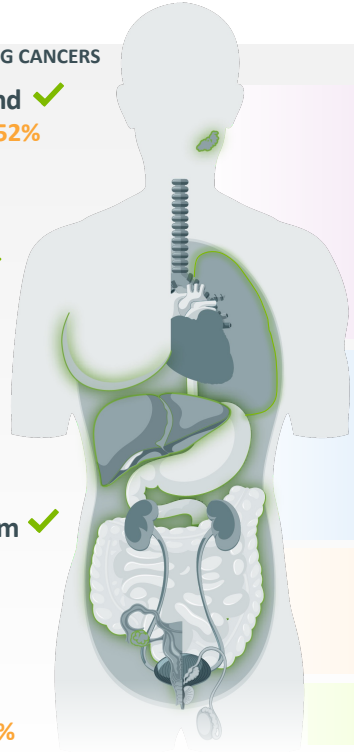
Broad Opportunities for Zanidatamab in HER2-Targeted Therapy

Leverage Jazz's integrated capabilities and global infrastructure to develop zanidatamab…

HER2 EXPRESSING CANCERS

- **Salivary Gland** ✓ — 17-44% | 12-52%
- **Lung** ✓ — 2.5% | 2-3%
- **Pancreas** ✓ — 26% | 2%
- **Bladder** — 12.4% | 9%
- **Ovarian** ✓ — 27% | 7%
- **Endometrium** ✓ — 18-80% | 4%
- **Prostate** — 10% | 6%
- **Cervix** — 21% | 0.5-14%



	PHASE 1	PHASE 2	PIVOTAL
Breast ✓ 15-20% | 20%	3L+ Zanidatamab + Ibrance (anti-CDK4/6) + Fulvestrant		
	1L Zanidatamab + Docetaxel		
	3L+ Zanidatamab + Evorpacept (CD47-blocker)		
	3L+ Zani + Chemo		
Stomach ✓ 20% | 11-16%	1L Zanidatamab + SOC Chemo ± Tislelizumab *vs* Herceptin + SOC Chemo (HERIZON)		
	1L Zanidatamab + SOC Chemotherapy + Tislelizumab		
	1L Zanidatamab + SOC Chemotherapy		
Biliary Tract ✓ 20% | 5-15%	2L Zanidatamab Monotherapy (HERIZON)		
	1L Zanidatamab + SOC (cisplatin + gemcitabine)		
Colorectal ✓ 5% | 6%	1L Zanidatamab + SOC (mFOLFOX6 ± bevacizumab)		

SOC = Standard of Care

HER2 EXPRESSION | AMPLIFICATION

ZANIDATAMAB SINGLE AGENT ACTIVITY ✓

… and create significant future upside to Zymeworks through milestones and royalties

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Modified from Oh D-Y & Bang Y-J 2019 Nat Rev Clin Onc

Zanidatamab Licensing Agreement: Key Financial Terms

	Licensing Agreement Terms[1]
Counterparty	Jazz Pharmaceuticals
Upfront Payments[2]	$375,000,000
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[3]
Future R&D Spend	Jazz to fund 100% of costs of future studies

Additional Details:

- Upfront payments[2] reflect $50MM one-time payment upon receipt of HSR Clearance and, at Jazz's option, $325MM after top-line HERIZON-BTC-01 data
- Ongoing zanidatamab related clinical studies and initial BLA to be managed by Zymeworks (100% of costs reimbursed)
- Future zanidatamab-related clinical studies, regulatory filings and commercialization to be managed and funded by Jazz
- Jazz to have exclusive license in US, EU, Japan and all other territories except those in Asia Pacific not covered by BeiGene agreement
- Zymeworks will continue to supply zanidatamab to Jazz for clinical and commercial use for at least two years (100% of costs reimbursed)

[1] All dollar values in US Dollars
[2] Zymeworks is eligible to receive a $50 million upfront payment, following receipt of the clearance relating to the United States Hart-Scott Rodino Antitrust Improvements Act of 1976 (such clearance, the "HSR Clearance"), and should Jazz decide to continue the collaboration following readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of $325 million
[3] Costs related to ongoing clinical studies incurred after signing of the agreement to be reimbursed 100% by Jazz

Zanidatamab Partnership Provides Renewed Focus and Clarity on Zymeworks' Corporate Strategy

Renewed Focus on Advancing and Maximizing Value from Early-stage Clinical Pipeline

- **Zanidatamab Zovodotin (ZW49)**: Enables focused spending to move program into a potential registrational study by 2025
- **Technology platforms**: Continued utilization of platforms to generate future best-in-class product candidates in Antibody Drug Conjugate (ADC) and Multi-specific Antibody Therapeutics (MSAT) research areas
- **Goal**: Advance 5 new product candidates into clinical studies within 5 years
  - Including advancing both ZW171 and ZW191 into the clinic by 2024

Clarity on Future Partnering & Collaborations Strategy

- **Achieve** ZW49 partnership prior to commencement of registrational studies
- **Target** partnerships for future product candidates in ex-US markets prior to registrational studies
- **Focus** on additional partnerships to generate and fund additional product candidates in both ADC and MSAT platforms
- **Leverage** early-stage collaborations to access technologies/programs that are complementary to in-house capabilities

Focused R&D to Help Drive Next Wave of Development for Difficult-to-Treat Cancers

Integrated R&D Engine

- Multi-specific Antibody Therapeutics (MSAT)
- Antibody Drug Conjugates (ADC)

Product Profile

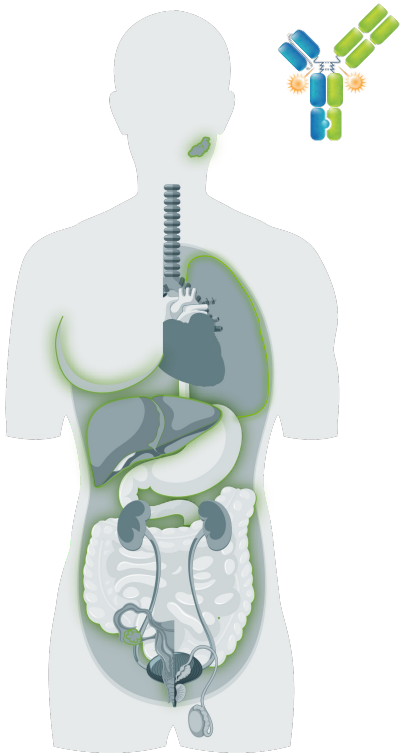
- First and Second-line opportunities
- Accelerated Approval regulatory pathway allows potential of early market entry

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

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

ADC: antibody-drug conjugate; OS: Overall Survival

Zanidatamab Zovodotin: Differentiated HER2-Targeted ADC



Zanidatamab zovodotin

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

Non-Small Cell Lung Cancer (NSCLC)

HER2-amplified, -expressing, and -mutated

Metastatic Breast Cancer (mBC)

HER2-positive mBC after previous treatment with T-DXd

HER2-low mBC

Gastroesophageal Adenocarcinoma (GEA)

Previously treated HER2-positive GEA

Other HER2-expressing Tumors

Ovarian, endometrial, bladder

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

Potential combinability with standards of care across indications, with no known overlapping toxicities

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

ADC: antibody drug conjugate

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Extended Cash Runway Allows Focus on Advancing Pipeline as Zanidatamab Advances to Commercialization

Updated Cash Runway Guidance

Significantly improved cash balance enables Zymeworks to fund planned operations **through at least 2026**

Cash Runway Guidance **Includes**:

- Receipt upfront payments[1] from Jazz and existing cash resources[2]
- Ongoing funding from Jazz for zanidatamab development
- Certain anticipated regulatory milestones from BGNE and JAZZ related to BTC and GEA
- Certain royalty payments for zanidatamab from Jazz
- Advancement of ZW49 into registrational studies
- Advancement of preclinical product candidates for two new INDs by 2024, plus one annually thereafter

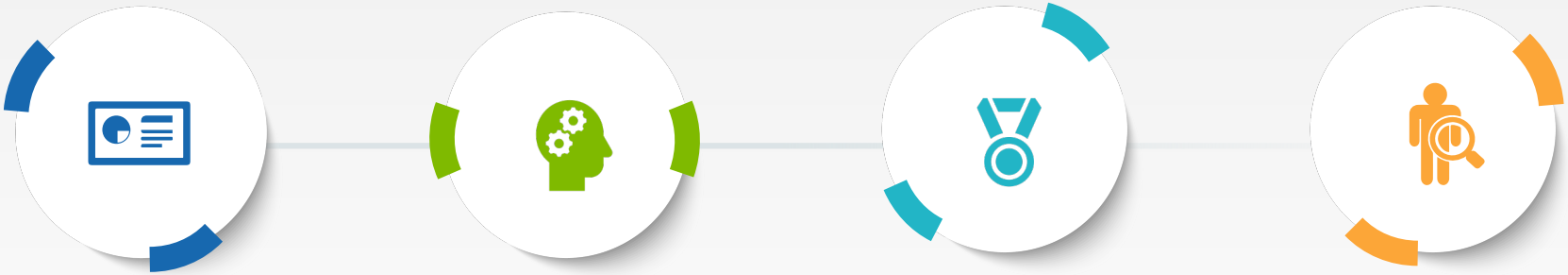
Cash Runway Guidance **Excludes**:

- Proceeds from additional partnerships
- Potential additional regulatory milestones for zanidatamab from BGNE and JAZZ
- Potential commercial milestones for zanidatamab
- Potential royalties for zanidatamab from BGNE

[1] Zymeworks is eligible to receive a $50 million upfront payment, following receipt of the clearance relating to the United States Hart-Scott Rodino Antitrust Improvements Act of 1976 (such clearance, the "HSR Clearance"), and should Jazz decide to continue the collaboration following readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of $325 million

[2] Zymeworks has reported cash resources of $241.8MM as of 6/30/2022

Key Expected Events & Milestones Throughout the Product Pipeline



4Q 2022

- **Early R&D Day** (October 20th)
- Late-Line **HR+ / HER2+ mBC** for zanidatamab
- **Recommended Phase 2 Dose** for zanidatamab zovodotin
- **HERIZON-BTC-01** Top-Line Data
- Expected close of JAZZ licensing agreement

1H 2023

- **HERIZON-BTC-01** Study Completion
- **Phase 2 1L GEA** Follow-Up (zanidatamab + chemotherapy)
- **Additional publications** on preclinical development candidates

2H 2023

- **HERIZON-GEA-01** Complete Patient Enrollment
- **Nomination** of next product candidate for Preclinical Development (PCD)

2024

- **Submit 2 IND Applications** for ZW171 and ZW191
- **HERIZON-GEA-01** Expect top-line data
- **Continue leveraging platforms** to generate preclinical product candidates and partnerships

HR+: Hormone receptor positive; IND: investigational new drug; OS: overall survival; PFS: progression-free survival

Key Transaction Benefits to Zymeworks

- **Meaningful improvement** to **financial position** and **reduction in future expenditures** allow Zymeworks to 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

Transaction allows zanidatamab to reach a broad group of patients globally and may potentially improve patient outcomes beyond the current standards of care

Selected Near-Term Upcoming Events for Zymeworks

1. Early R&D Day in New York City on October 20th
2. Q3 Earning Results scheduled for November 8th
3. SITC poster on TLR7 ADC abstract on November 10th
4. Stifel Healthcare Conference in NYC on November 16th
5. Jefferies Healthcare Conference in London on November 15th - 16th
6. Spotlight poster presentation for zanidatamab in mBC at SABCS on Dec 9th
7. Determination of RP2D for zanidatamab zovodotin (ZW49) by the end of 2022
8. Top-line data announcement for registrational study of zanidatamab as monotherapy in 2L+ BTC patients by the end of 2022
9. Expected closing of licensing agreement with Jazz Pharmaceuticals by the end of 2022
10. Updated corporate goals and financial guidance for 2023 (early 2023)

mBC: metastatic breast cancer; RP2D: Recommended Phase 2 dose; SABCS: San Antonio Breast Cancer Symposium; SITC: Society for Immunotherapy of Cancer's annual meeting; TLR7: toll-like receptor 7

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