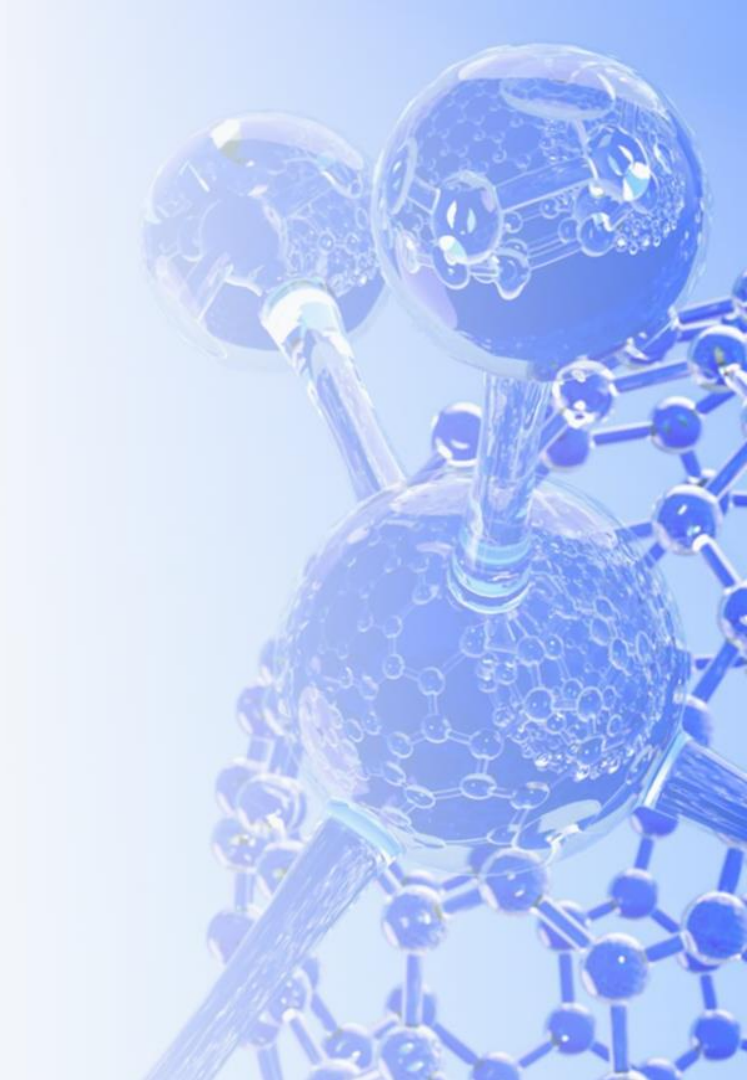
4Q & FY 2022 Results Conference Call and Webcast

March 7, 2023



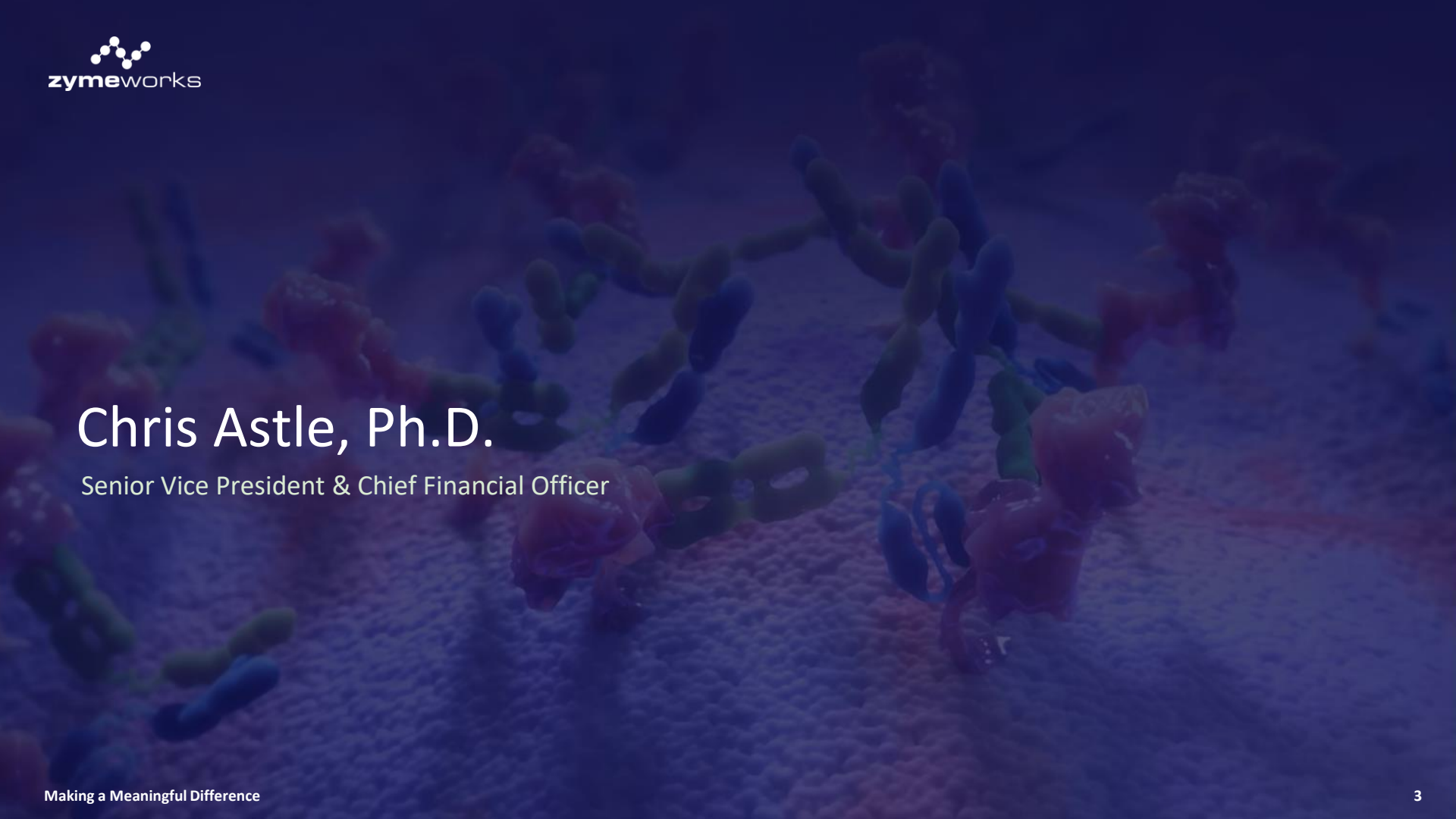
Nasdaq: ZYME | zymeworks.com

Forward-Looking Statements

This presentation and the accompanying oral commentary include “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 may relate to our expectation regarding implementation of our strategic priorities and meeting expected timelines; the clinical development of our product candidates and enrollment in our clinical trials; anticipated clinical data presentations, including the expected presentation of full results from HERIZON-BTC-01 in 2023, and the timing thereof; anticipated therapeutic effects and commercial potential of our current and future product candidates; expected financial performance and future financial position; anticipated continued receipt of revenue from existing and future partners; our preclinical and early stage pipeline and the advancement of such pipeline; our ability to execute new collaborations and partnerships; advancement of zanidatamab zovodotin into registrational studies and other product candidates in clinical studies; our ability to satisfy potential regulatory and commercial milestones with existing and future partners; the timing and status of ongoing and future studies and the related data; the timing of and results of interactions with regulators; the anticipated benefits of the collaboration agreement with Jazz, including Zymeworks’ ability to receive any future milestone payments and royalties thereunder; our anticipated net operating cash burn and planned capital expenditures in 2023; anticipated sufficiency of cash resources and other potential sources of cash, including anticipated payments from Jazz, to fund our planned operations through at least 2026, and potentially beyond; expectations regarding future regulatory filings and approvals and the timing thereof and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “subject to,” “anticipate,” “plan,” “expect,” “estimate,” “project,” “may,” “will,” “should,” “would,” “could,” “can,” 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, our examination of historical operating trends, are based upon our current expectations and various assumptions. We believe there is a reasonable basis for our expectations and beliefs, but they are inherently uncertain. We may not realize our expectations, and our 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 our or our collaborators’ product candidates; any of our or our 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; we may not be able to achieve additional milestones and receive related payments and royalties from our existing or future collaborations; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; our assumptions regarding our financial condition or future financial performance may be incorrect; we may not be able to maintain or enter into new partnerships or strategic collaborations; the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; Zymeworks may not recognize the anticipated cost savings and related benefits of its 2022 reduction in workforce and other factors described in the "Risk Factors" and other sections of our public filings with the Securities and Exchange Commission and Canadian securities regulators.

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.



Chris Astle, Ph.D.

Senior Vice President & Chief Financial Officer

Full Year 2022 Financial Results

In millions USD	Full Year 2021	Full Year 2022
Revenue	$26.7	$412.5
R&D Expense	$199.8	$208.6
G&A Expense	$42.6	$73.4
Net Income (Loss)	($211.8)	$124.3
Cash Resources[1]	$252.6	$492.2

Net Operating Cash Burn Guidance

Expect between $90 - $120 million for calendar year 2023

- **Revenue** in 2022 primarily driven by $375MM in upfront payments and approximately $24MM in zanidatamab related reimbursements
- **R&D Expense** increase primarily driven by higher manufacturing and clinical trial expenses for zanidatamab and partially offset by a decrease in expenses for preclinical and zanidatamab zovodotin related activities in 2022
- **G&A Expense** increase primarily driven by an increase in consulting and professional fees, including fees related to the, Jazz collaboration agreement, depreciation expenses, and other expenses incurred related to our 2022 reduction in force and was primarily offset by a decrease in salaries and benefits related to our 2022 reduction in force
- **Net Income** of $1.90 per fully diluted share is first annual income generated since Company's incorporation
- **Cash Resources**[1] are anticipated to fund our planned operations through at least 2026, and potentially beyond

R&D: research and development; G&A: general and administrative; USD: United States dollar

[1] Cash resources consist of cash, cash equivalents, and short-term investments.

Note: All financial results are as-reported for the years ended December 31, 2021, and December 31, 2022, respectively.

Five by Five: Delivering on a Focused Early Research and Development Strategy

Early Research and Development Pipeline

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, NSCLC, TNBC

Additional TOPO1 ADCs

Additional TriTCEs/MSATs

- **Focused strategy** to have five novel preclinical product candidates in clinical studies by 2027
- Both ZW191 and ZW171 are **on track for IND in 2024**
- **Acceptance of 11 abstracts at AACR** to continue advancing preclinical candidates towards future INDs
- Anticipate nominating **one additional preclinical candidate** this year for IND submission in 2025
- **Partnership and business development strategy important** as we advance additional product candidates beyond 5x5
- Expect to complete **additional collaboration and partnerships** for multiple preclinical candidates this year

CRC: Colorectal cancer; GEA: gastroesophageal adenocarcinoma; IND: investigational new drug; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer

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)

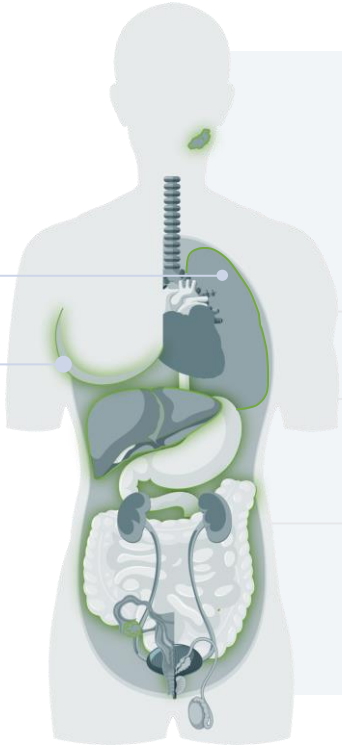
HER2-targeted NSCLC

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 expected 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

Potential combinability 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: Recent Data Continues to Support Potential Best-in-Class HER2-targeted therapy in BTC and GEA

HERIZON-BTC-01
December 2022 Top-line data

- cORR of 41.3% [95% CI: 30.4, 52.8]
- mDOR of 12.9 months [95% CI: 5.95, NE]
- Safety profile was consistent with previously reported zanidatamab monotherapy studies with no new safety signals
- Full clinical data expected to be presented in 1H-23

Phase 2 data (NCT04466891) as reported in Company press release | Dec 2022

Updated Phase 2 data in 1L GEA
ASCO Gastrointestinal Cancers Symposium Data Presentation

- 84% [95% CI: 68, 93] overall survival at 18 months, median not yet reached
- cORR of 79% [95% CI: 63, 90%]
- mPFS of 12.5 months [95% CI: 7.1, NE]
- mDOR of 20.4 months [95% CI: 8.3, NE]
- Regimen was manageable, tolerable, and consistent with prior zanidatamab results in GEA patients

Phase 2 data (NCT03929666) as reported at ASCO GI | Jan 2022

Zanidatamab has shown **broad activity in HER2-expressing cancers** and **path forward for indications beyond BTC and GEA** to be determined by ongoing development efforts

BTC: biliary tract cancer; cORR: confirmed objective response rate; DCR: disease control rate; GEA: gastroesophageal adenocarcinoma; mDOR: median duration of response; mPFS: median progression-free survival;

Enterprise Value Framework

Our Strategy

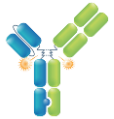
Zymeworks is well-positioned to build upon our key priorities and enhance shareholder value through focusing on our Enterprise Value Framework

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

Global[1] Zanidatamab Collaboration with Jazz Pharmaceuticals

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

Q&A

Kenneth Galbraith
Chair and CEO

Neil Klompas
President and COO

Chris Astle, Ph.D.
SVP and CFO

Paul Moore, Ph.D.
CSO