# zymeworks

## Making Therapies that Make a Difference

**CORPORATE OVERVIEW** 

**NYSE: ZYME** 

www.zymeworks.com

### Legal Disclaimer

This presentation includes "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward looking statements. Forward-looking statements include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as "subject to," "believe," "anticipate," "plan," "expect," "intend," "estimate," "project," "may," "will," "should," "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, projectives, 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 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 risks and uncertainties, including those described in the "Risk Factors" and other sections of our public filings with the Securities and Exchange Commission and Canadian securities regulators.

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### Leading the Next Wave of Biotech Breakthroughs



#### Paradigm Shift Towards Multifunctional Therapeutics

The future of drug development lies in therapeutics that target diseases with multiple mechanisms of action

# Zymeworks is Leading the Wave of Multifunctional Drug Development

Zymeworks is at the forefront of this paradigm shift by developing multifunctional therapeutics through its proprietary platforms

#### Fully-Integrated, Self-Sustaining Biotech Leader

Zymeworks' novel platforms and robust pipeline combines to drive continuous growth and innovation with a focus on clinical outcomes and patients





### Zymeworks' Robust Pipeline of Potential



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\*BeiGene to develop and commercialize in Asia Pacific countries including China, South Korea, Australia, and New Zealand but excluding Japan.

### Partnerships & Collaborations Advancing into the Clinic



•Original Agreement with Celgene (which is now a Bristol-Myers Squibb company) •Original Agreement with Iconic; XB002 in-licensed by Exelixis



### **Active Partnerships with Global Pharmaceutical Leaders**

						Potential Remaining	
PARTNER	EVENTS	PLATFORMS	PROGRAMS/ASSETS	\$ RECEIVED	MILESTONES	ROYALTY %	
	Announced: 2011 Milestone: #3 2019 Expanded: 2020		Up to 4	7.0	951.0	Low-Mid Single Digit	
Lilly	Announced/Expanded: 2014 Milestones 1/2: 2015/2016 Filed 2 INDs: 2018/2019		Up to 2	14.0	163.0	Low-Mid Single Digit	
Celgene t <sup>th</sup> Bristol Myers <sup>+</sup> Squibb <sup>+</sup>	Announced: 2015 Milestone 1: 2019 Extended: 2018/2020		Up to 10	31.5	1.63B	Low-Mid Single Digit	
gsk	EFECT Announced: 2015 Azymetric: Announced 2016 Azymetric: Expanded: 2019		AZYMETRIC Up to 6 EFECT Up to 10	6.0	2.18B	Low-Mid Single Digit	
Daiichi-Sankyo	Announced: 2016 Milestones 1/2: 2017/2019 Expanded: 2018		Up to 3	24.5	610.1	Low Single Digit to 10	
Johnson-Johnson Innovation	Announced: 2017		Up to 6	50.0	1.40B	Mid Single Digit	
LEO	Announced: 2018		Up to 2	5.0	474.5	High Single Digit-20*	
BeiGene	Announced: 2018 Milestone: 2020		Zanidatamab <sup>^</sup> Up to 3 ZW49 <sup>^</sup>	75.0	1.08B	Tiered up to 20**	
	Announced: 2019 In-licensed by Exelixis: 2020		XB002 (formerly ICON-2) Tissue Factor ADC	Undisclosed/Rev Share	Undisclosed/Rev Share	Mid Single Digit	
All amounts are in US\$ millions unless otherwise indicated			Up to 47	\$213M	Up to \$8.6B		

^Development and commercial rights in CN, KR, AU, NZ + other countries. \*Original Agreement with Celgene (which is now a Bristol-Myers Squibb company)

\*1<sup>st</sup> product: high single digit-20% in US, mid-high single digit ex-US & 2<sup>nd</sup> product: high single-low double digit worldwide \*\*up to 20% in BeiGene territory for Zanidatamab/ZW49, tiered mid-single digit worldwide for BeiGene Azymetric/EFECT products

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6 \*\* Original Agreement with Iconic; XB002 in-licensed by Exelixis

### Novel Platforms Enable First & Best-in-Class Multifunctional Therapeutics

#### Our approach to platform development:

#### Azymetric™

#### Bispecific Antibody Platform

- Dual targeting of receptors and ligands
- IgG1-like biophysical and functional properties
- IgG1-like manufacturing and purification protocols



#### ZymeLink™

Next-Gen Drug Conjugate Platform

Suite of proprietary toxins

• IgG1-like PK and exposure

Demonstrated tolerability

Wide therapeutic window

Stable, cleavable linkers



#### EFECT™

#### Immune Function Modulating Platform



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



### Powerful Platforms that Enable Tailor-Made Biotherapeutics



### Fully-Integrated Drug Development Engine



### Dual-Drug Approach to Address HER2-Expressing Cancer Spectrum



#### Zanidatamab (ZW25) Bispecific HER2 Antibody

- Multiple MOAs to eliminate HER2 signaling
- Combines well with SOC for early lines of therapy
- Cytotoxin-free approach for fragile patients

#### **ZW49**

#### Bispecific HER2 Antibody-Drug Conjugate

- Uses HER2 expression to deliver cytotoxin
- Later-stage and/or lower HER2-expressing tumors
- Broad therapeutic window in preclinical studies



### Zanidatamab Could Displace Herceptin ± Perjeta as the Foundational **Treatment for HER2-Expressing Cancers**

Herceptin ± Perjeta is Currently the Foundational Regimen to Treat HER2+ Breast Cancer



### Opportunities for Zanidatamab & ZW49 in Many HER2 Cancers

APPROVED HER2 AGENTS	ZANIDATAMAB SINGLE AGENT ACTIVITY	HER2 EXPRESSING CANCERS		ZANIDATAMAB SINGLE AGENT ACTIVITY	APPROVED HER2 AGENTS	
	<ul> <li>Image: A second s</li></ul>	Salivary Gland 17-44%   12-52%	Lung 2.5%   2-3%			
Herceptin Perjeta Kadcyla Tykerb Nerlynx Enhertu Tukysa Margenza	<ul> <li>Image: A second s</li></ul>	Breast 15-20%   20%	Stomach 20%   11-16%	<ul> <li>Image: A second s</li></ul>	Herceptin Enhertu	
	<ul> <li>Image: A second s</li></ul>	Biliary Tract 20%   5-15%	Pancreas 26%   2%	<ul> <li>Image: A second s</li></ul>		
	×	Ovarian 27%   7%	Colorectum 5%   6%	<ul> <li>Image: A second s</li></ul>		
	~	Endometrium 18-80%   4%	Bladder 12.4%   9%			
		Cervix 21%   0.5-14%	Prostate 10%   6%			





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

### Potential Markets for Zanidatamab & ZW49 in Gastric & Breast Cancer



**Expanding the Treatment Paradigm for HER2+ Cancer** 



### Zanidatamab (ZW25): Bispecific Antibody for HER2-Expressing Cancers

Unique Mechanisms of Action

Clinical

Highlights

Trial

- Biparatopic targets two distinct HER2 epitopes
- Increased tumor cell binding
- Enhanced HER2 internalization and down-regulation
- Potent effector-mediated cytotoxicity
- Blocks ligand-dependent and -independent tumor growth

Clinical benefit<sup>1</sup> observed across multiple HER2-expressing tumor types

- Zanidatamab + chemo shows durable activity in heavily pretreated patients
- FDA Breakthrough Therapy designation for pivotal trial in 2<sup>nd</sup> line biliary tract cancer
- Initiated P2: Zanidatamab + SOC chemo in 1<sup>st</sup> line gastroesophageal adenocarcinoma (GEA)
- Initiated P2: Zanidatamab + Ibrance (CDK4/6 inhibitor) + fulvestrant in HR+ breast cancer
- Planned: Zanidatamab + ALX148 (CD47 blocker) in HER2 high and HER2 low breast cancer

Expected Zanidatamab Catalysts

- 1H 2021 Initiate multiple new clinical trials in breast cancer
- 1H 2021 Report P2 data from 1st line GEA trial
- Mid-2021 Initiate 2<sup>nd</sup> pivotal study in 1<sup>st</sup> line HER2+ GEA
  - Zanidatamab + chemotherapy ± tislelizumab vs. Herceptin + chemotherapy



<sup>1</sup> Confirmed partial response or stable disease ≥ 6 months

### Dual HER2-Binding of Zanidatamab Drives Unique MOA

#### Zanidatamab's unique binding geometries promote:

- Extended chain formation and HER2 receptor clustering
- Enhanced HER2 internalization and downregulation
- Increased tumor cell binding density and potent effector function-mediated cytotoxicity
- Enhanced blockade of ligand-dependent and ligand-independent tumor growth



Monoclonal Binding – Each HER2 receptor can only be bound by one monoclonal antibody



MOA: Mechanism of Action

### Zanidatamab Monotherapy Anti-Tumor Activity in BTC



E = Extrahepatic Cholangiocarcinoma, FISH = fluorescence in situ hybridization; I = Intrahepatic Cholangiocarcinoma; IHC = immunohistochemistry; G = Gallbladder; T = trastuzumab; Trt = treatment. Response-evaluable: all treated patients with measurable disease who had at least one evaluable, post-baseline disease assessment (per RECIST 1.1) or discontinued study treatment due to death or clinical progression. Note: One patient was not response evaluable because they withdrew from the study. One patient in the response-evaluable set died prior to the post-baseline tumor measurement and is not included in the plot (counted as PD). Data snapshot from unlocked database 16 November 2020 and subject to change.



### Duration of Treatment for Zanidatamab Monotherapy in BTC



#### Median Duration of Response: 7.4 months (95% CI; 3.2, NE)

(c)PR = (confirmed) partial response; E = extrahepatic cholangiocarcinoma, FISH = fluorescence in situ hybridization; I = intrahepatic cholangiocarcinoma, IHC = inmunohistochemistry; G = gallbladder; PR = partial response; PD = progressive disease; SD = stable disease; T = trastuzumab; Tx = Treatment. \*, death. Data snapshot from unlocked database 16 November 2020 and subject to change.



### Zanidatamab Monotherapy Anti-tumor Activity in GEA



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### Zanidatamab Monotherapy Duration of Treatment in GEA





### Addition of Chemo to Zanidatamab Increases Response in GEA



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#### Promising activity seen in patients with FISH+ and FISH- disease

#### Zanidatamab + Chemo Duration of Treatment





Months

### Zanidatamab Clinical Development – Priority Studies





### ZW49: Bispecific ADC for HER2-Expressing Cancers

Catalysts

Biparatopic-induced internalization Unique Increased toxin-mediated cytotoxicity Enhanced platform tolerability **Mechanisms** Broad therapeutic window of Action Potential to address unmet need in high and low HER2-expressing • cancers, including brain metastases Multiple confirmed responses and stable disease observed in several tumor types • Clinical • Differentiated safety profile with the majority of adverse events grade 1 or 2, reversible and Data manageable Expansion cohorts open and enrolling patients at 2.5 mg/kg once every three weeks **Highlights**<sup>1</sup> Maximum tolerated dose not established, dose escalation continuing in parallel Expected Complete expansion cohorts & select recommended Phase 2 dose **ZW49** 

• 2H – Report Ph1 clinical data at medical meeting



ZW49 – Internalizes and Releases Toxin Intracellularly in HER2-Expressing Cells to Greater Levels than Monospecific ADC Leading to Improved Cytotoxicity





### ZW49: Efficacy Competitive vs Approved HER2-Targeted ADCs



#### **Zymeworks Priorities**

- Complete enrolment of zanidatamab pivotal trial in HER2-amplified biliary tract cancer
- Launch pivotal trial in 1<sup>st</sup> line HER2-positive GEA, and present supporting Phase 2 clinical data

#### **Corporate Highlights**

#### Zanidatamab (ZW25)

- ✓ Zanidatamab +/- chemo presented at ASCO GI; Durable activity in BTC and GEA; supports pivotal trials in 2<sup>nd</sup> & 1<sup>st</sup> line, respectively
- ✓ FDA granted Breakthrough Therapy designation for BTC
- ✓ Pivotal trial initiated in refractory BTC; targeting BLA in 2022
- ✓ P2 trials initiated in 1st line Breast (with chemo) and 1st line GEA (with anti-PD1 and chemo) by partner BeiGene
- Monotherapy presented at ESMO Asia; Durable disease control across tumors; supports pivotal trial in 2<sup>nd</sup> line biliary tract cancer

#### ZW49

- ✓ Confirmed responses & stable disease in several tumor types
- ✓ Majority of AEs Gr 1/2, reversible and manageable
- ✓ Expansion cohorts open & enrolling; MTD not established

- Present data to support zanidatamab breast cancer development strategy
- Advance ZW49 into and complete cohort expansion
- Present data from new therapeutic programs and technology platforms

#### PARTNERSHIPS

- ✓ XB002 Iconic TF-targeting ZymeLink™ ADC in-licensed by Exelixis; ZW receives share of \$20M option fee, future revenues, & tiered royalties
- Expansion of Zanidatamab pivotal BTC trial in Asia with BeiGene; Zymeworks receives \$10M milestone payment
- ALX Oncology collaboration; Zanidatamab + ALX148 (CD47 blocker) in advanced HER2-expressing breast cancer
- Merck signs new Azymetric and EFECT licenses; up to \$411M in development and up to \$480M in commercial milestones
- ✓ BMS expands collaboration; gained access to the EFECT™ platform; ZW receives \$12M upfront
- Pfizer collaboration; initiation of P2 trial of Zanidatamab + Ibrance<sup>®</sup> + Fulvestrant in HER2+, HR+ metastatic breast cancer



#### Leadership Team



BC Premier's Tech Council. and MITACS and BIOTECanada's Advisory Boards and Committees. Ph.D. (Microbiology & Immunology) from UBC, M.Sc. (Biochemistry) from UMass.

Berlex and Immunex. Internal medicine and specialty training at University of Washington. M.D. from University of Pennsylvania and A.B. (Biology) from Princeton University.

Biotech/Pharma M&A Transaction Advisory Group & KPMG's Canadian Life Sciences practice.

Innovation Unit at Amgen. BSc (Pharmacology) from Adelaide University and Ph.D. (Biochemistry) from Flinders University (Adelaide).

and Vice President and Chief Human Resources Officer at PATH.

in strategic and operational Myers Squibb, and Amgen. He was Global Product General Manager for Kyprolis<sup>®</sup> and the entire Mveloma Portfolio. MBA from the NFOMA Business School in France.





#### **Board of Directors**

