

# Making Therapies that Make a Difference

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**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

#### Late Stage Clinical Pipeline: Lead Asset in Two Pivotal Trials

Lead asset, zanidatamab, is a bispecific antibody with potential to become a new foundational HER2-targeted therapy



### Zymeworks' Clinical Pipeline

Zanidatamab Advancing in Two Pivotal Trials with Broad Opportunity for Additional Indications



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



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# Partnerships & Collaborations Advancing into the Clinic

PROGRAMS   PLATFORMS		TFORMS	PRECLINICAL	PHASE 1	PHASE 2	COMMERCIAL RIGHTS
	PARTNERSHIPS					
	Bispecific Antibody		Oncology			<mark>رالا</mark> Bristol Myers* Squibb
	XB002 ( <i>ICON-2)</i> Tissue Factor ADC		Solid Tumors			EXELI <mark>X</mark> IS <sup>**</sup>
	JNJ-78278343 CD3 x KLK2 Bispecific		Castration-Resistant Prostate Cancer			<b>Јоћтоп-Јоћтоп</b> иночетон
	JNJ-78306358 CD3 x HLA-G Bispecific		Solid Tumors			<b>Јонтоп «Јонтоп</b> иночетон
	Bispecific Antibody		Undisclosed			
	Bispecific Antibody		Immuno-Oncology			Dauchi-Saniyo
	Bispecific Antibody		Infectious Disease/Undisclosed			gsk
	Bispecific Antibody		Dermatology			
	Bispecific Antibody		Undisclosed			🔁 BeiGene
	Azymetric	c EFECT ZymeLink	c ment with Celgene (which is now a Bristol-Myers Squibb com	ipany)		A.C.
5		y Original Agree	ment with forme, Abooz m-neelised by Exelixis			Zymeworks

### Active Partnerships with Global Pharmaceutical Leaders

#### \$225MM+ in Partnership Revenue Received with \$8.5B+ in Total Deal Value

PARTNER	EVENTS	PLATFORMS	PROGRAMS/ASSETS	TOTAL DEAL VALUE	ROYALTY %
	Announced: 2011 Milestone: #3 2019 Expanded: 2020		Up to 3	\$891	Low-Mid Single Digit
ر <sup>ال</sup> ا، Bristol Myers⁺ Squibb	Announced: 2015 Milestone 1: 2019 Extended: 2018/2020		Up to 10	\$1.66B	Low-Mid Single Digit
gsk	EFECT Announced: 2015 Azymetric: Announced 2016 Azymetric: Expanded: 2019		AZYMETRIC Up to 6 EFECT Up to 10	\$2.19B	Low-Mid Single Digit
Dailchi-Sankyo	Announced: 2016 Milestones 1/2: 2017/2019 Expanded: 2018		Up to 3	\$635	Low Single Digit to 10
Johnson Johnson Innovation	Announced: 2017 First Asset Phase 1 Milestone: 2021 Second Asset Phase 1 Milestone: 2021		Up to 6	\$1.45B	Mid Single Digit
	Announced: 2018		Up to 2	\$480	High Single Digit-20*
🔀 BeiGene	Announced: 2018 First Pivotal Milestone: 2020 Second Pivotal Milestone: 2021		Zanidatamab <sup>^</sup> ZW49 <sup>^</sup> Up to 3	\$1.15B	Tiered up to 20**
EXELIXIS"	Announced: 2019 In-licensed by Exelixis: 2020 IND Filed: 2021		XB002 Tissue Factor ADC	Undisclosed / Rev Share	Mid Single Digit
All amounts are in US\$ millions unless other	wise indicated	Azymetric EFECT ZymeLink	Up to 46	More Than \$8.5B	

<sup>A</sup>Development and commercial rights in CN, KR, AU, NZ + other countries. <sup>+</sup>Original Agreement with Celgene (which is now a Bristol-Myers Squibb company) <sup>++</sup>Original Agreement with Iconic; XB002 in-licensed by Exelixis \*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



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

EFECT™

**Immune Function** 

**Modulating Platform** 

#### Our approach to platform development:



Bispecific Antibody Platform

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



- Suite of proprietary toxins
- Stable, cleavable linkers
- IgG1-like PK and exposure
- Demonstrated tolerability
- Wide therapeutic window

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



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



# Powerful Platforms that Enable Tailor-Made Biotherapeutics



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# Fully-Integrated Drug Development Engine



zvmeworks

### 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 and 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%	<ul> <li>Image: A second s</li></ul>	
Herceptin Perjeta Kadcyla Tykerb Nerlynx Enhertu Tukysa Margenza	~	Breast 15-20%   20%	Stomach 20%   11-16%	~	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%		



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



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



#### Zanidatamab: A Bispecific Antibody for HER2-Expressing Cancers

	Unique Mechanisms of Action	<ul> <li>Biparatopic - targets two distinct HER2 epitopes and results in</li> <li>HER2 binding across a range of expression levels (low to high);</li> <li>HER2-receptor clustering, internalization, and downregulation;</li> <li>Inhibition of growth factor-dependent and -independent tumor cell proliferation;</li> <li>Potent antibody-dependent cellular cytotoxicity and phagocytosis, and complement-dependent cytotoxicity</li> </ul>
HEROA HODE	Clinical Trial Highlights	<ul> <li>Clinical benefit<sup>1</sup> observed across multiple HER2-expressing tumor types</li> <li>Zanidatamab + chemo shows durable activity in heavily pretreated patients</li> <li>FDA Breakthrough Therapy designation for pivotal trial in 2<sup>nd</sup> line biliary tract cancer</li> <li>1L HER2+ GEA zanidatamab + chemo compares favorably to SOC; supports pivotal trial</li> <li>Initiated 2<sup>nd</sup> pivotal study of zanidatamab + tislelizumab + chemo in 1L+ line HER2+ GEA</li> <li>3L+ HER2+ breast cancer zanidatamab + chemo compares favorably to SOC</li> </ul>
	Expected Zanidatamab	<ul> <li>1H 2022: 1L HER2+ GEA   zanidatamab + chemo + tislelizumab</li> <li>1H 2022: 1L HER2+ breast cancer   zanidatamab + docetaxel</li> <li>1H 2022: 3L+ HER2+ HR+ breast cancer   zanidatamab + Ibrance (anti-CDK4/6) + fulvestran</li> </ul>

• Mid-2022: Complete enrollment for the HERIZON-BTC-01 pivotal clinical study



**Catalysts** 

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

#### Zanidatamab's unique binding geometry promotes:

- Binding to HER2 across a range of expression levels (low to high)
- HER2-receptor clustering, internalization, and downregulation
- Inhibition of growth factor-dependent and -independent tumor cell proliferation
- Antibody-dependent cellular cytotoxicity and phagocytosis; and complement-dependent cytotoxicity



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



MOA: Mechanism of Action

#### Zanidatamab Monotherapy in HER2-Expressing Late-Line BTC

As reported at ASCO GI | Jan 2021

Potential to be First HER2-Targeted Therapy Approved for Biliary Tract Cancer Patients



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.



Percent Change from Baseline in Sum of Diameters

### Zanidatamab Monotherapy in HER2-Expressing Late-Line BTC

As reported at ASCO GI | Jan 2021

Data supports pivotal trial with FDA Breakthrough Therapy Designation now enrolling in 2L+ BTC



(c)PR = (confirmed) partial response; E = extrahepatic cholangiocarcinoma, FISH = fluorescence in situ hybridization; I = intrahepatic cholangiocarcinoma, IHC = immunohistochemistry; 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 Plus Chemotherapy in HER2+ First-Line GEA

As reported at ESMO | Sep 2021

#### 93% cORR for Proposed Phase 3 Regimen (zanidatamab + CAPOX or FP)



<sup>2</sup>HER2-positive was defined as IHC 3+ or IHC 2+/FISH+.<sup>b</sup>CORR included a baseline scan and a confirmatory scan obtained ≥ 4 weeks following initial documentation of objective response; the efficacy-evaluable population was defined as all HER2-positive subjects who had ≥ 1 evaluable post-baseline disease assessment or discontinued study treatment due to death or clinical progression.

5-FU = 5-fluorouracii; CAPOX = capecitabine plus oxaliplatin; cORR = confirmed objective response rate; CR = complete response; DCR = disease control rate; E = esophageal cancer; F = flat dosing; FISH = fluorescence in situ hybridization; FP = 5-FU and cisplatin; G = gastric cancer; IHC = immunohistochemistry; J = gastroesophageal junction cancer; mFOLFOX6 = 5-FU plus oxaliplatin and leucovorin; NR = not reached; ORR = objective response rate (CR + PR); PD = progressive disease; PR = partial response; SD = stable disease; W = weight-based dosing; ZDR = zanidatamab dosing regimen.



#### Zanidatamab Plus Chemotherapy in HER2+ First-Line GEA

As reported at ESMO | Sep 2021

#### Median Progression Free Survival of 12.0 months

CA ZDR FISH IHC



\* An MRI performed for neurologic symptoms on Day 8 demonstrated brain metastases, which were treated with radiation therapy. Subject remained on mFOLFOX6-1 with zanidatamab and has had long term disease control since treatment of brain metastases.

5-FU = 5-fluorouracil; CA, primary tumor location; CAPOX = capecitabine plus oxaliplatin; cCR = confirmed CR; CR = complete response; cPR = confirmed PR; DOR = duration of response; E = esophageal cancer; F = flat dosing; FISH = fluorescence in situ hybridization; FP = 5-FU plus cisplatin; G = gastric cancer; IHC = immunohistochemistry; J = gastroesophageal junction cancer; mFOLFOXG = 5-FU plus oxaliplatin and leucovorin; NR = not reached; PD = progressive disease; PR = partial response; SD = stable disease; W = weight-based dosing; ZDR = zanidatamab dosing regimen; + = indicates that the subject is in response at the time of data extraction.



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#### Zanidatamab Plus Chemotherapy in HER2+ 3L+ Breast Cancer

As reported at SABCS | Dec 2021

Promising antitumor activity observed in heavily pretreated breast cancer patients



C = tucatinib; cORR = confirmed objective response rate; cPR, confirmed partial response; DOR = duration of response; DCR = disease control rate; FISH = fluorescence in situ hybridization; HR = hormone receptor; IHC = immunohistochemistry; K = T-DM1; L = lapatinib; N = neratinib; P = pertuzumab; Tr = treatment

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

Biparatopic-induced internalization Unique Increased toxin-mediated cytotoxicity **Mechanisms** Enhanced platform tolerability of Action Broad therapeutic window • Potential to address unmet need in high and low HER2-expressing • cancers, including brain metastases HERZA 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 Maximum tolerated dose not established, dose escalation continuing in parallel

> Expected ZW49 Catalysts

- Complete expansion cohorts & select recommended Phase 2 dose
- Report Phase 1 clinical data at medical meeting in 2022



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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



# Key Strategic Priorities for 2022 to 2023

#### Clinical

- Fully recruit the HERIZON-BTC-01 pivotal clinical study for zanidatamab by mid-2022
- Fully recruit the HERIZON-GEA-01 pivotal clinical study for zanidatamab by the end of 2023
- Complete or close out other ongoing early-stage clinical studies for zanidatamab as data become available; data will help to identify and support strategic decisions regarding future clinical development opportunities beyond the ongoing pivotal clinical studies
- Finalize a clear clinical development path for ZW49 based on additional clinical data expected in 2022

#### **Preclinical and R&D**

- Select and advance two new antibody-drug conjugate or multispecific product candidates leveraging Zymeworks' novel, therapeutic platforms (Azymetric<sup>™</sup>, ZymeLink<sup>™</sup>, EFECT<sup>™</sup> and ProTECT<sup>™</sup>) to IND-enabling studies to provide the ability to submit two Investigational New Drug (IND) applications by the end of 2024
- Continue to support and advance Zymeworks' core technology platforms and collaborations

#### **Partnering & Finance**

- Execute on new partnerships and collaborations to support the development and commercialization of zanidatamab and Zymeworks' early-stage R&D pipeline and technology platforms
- Improve Zymeworks' financial position over 2022 and 2023 through a combination of alternatives, including forming additional partnerships and collaborations, monetizing existing assets and products and securing additional financing.



#### Leadership Team





#### **Board of Directors**

