

# Zymeworks Inc.

ZYME-NYSE | ZYME-TSX

David Novak MSc | 416.777.7029 | david.novak@raymondjames.ca

Biotechnology

March 19, 2018 | 5:15 am EDT  
Company Report - Initiation of Coverage

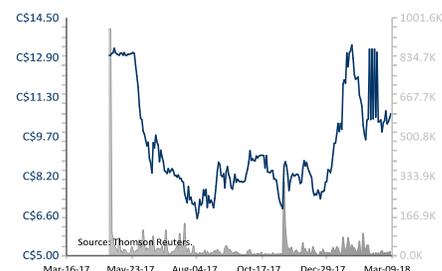
## Outperform 2 US\$18.00 target price

Current Price ( Mar-15-18 )	US\$11.05
Total Return to Target	66%
52-Week Range	US\$14.25 - US\$6.25
Suitability	High Risk/Speculation

<b>Market Data</b>	
Market Capitalization (mln)	US\$276
Current Net Debt (mln)	US\$0
Enterprise Value (mln)	US\$188
Shares Outstanding (mln, f.d.)	28.4
10 Day Avg Daily Volume (000s)	21
Dividend/Yield	US\$0.00/0.0%

<b>Key Financial Metrics</b>			
	2017A	2018E	2019E
P/E Ratios (GAAP)			
	NM	NM	NM
Shares Outstanding (mln, basic)			25.5
BVPS			US\$2.91
LT Debt (mln)			US\$0
% Cap			0%

**Company Description**  
Zymeworks is a clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization of next-generation multifunctional biotherapeutics.



## Initiating Launch Of Canada's M.O.A.B.

### Recommendation

We are initiating coverage of Zymeworks Inc. with an Outperform rating and an US\$18.00 target price (High Risk/Speculation suitability, given ZYME's current stage of clinical development). Looking back at 2016, seven of the top ten innovative drugs worldwide were biologics, six of which were antibody-related molecules. In our view, antibody-based therapeutics will continue to dominate modern medicine, with bispecific antibody development holding significant promise. With robust platform technologies which have garnered significant partner interest, in addition to a growing pipeline of wholly owned assets, we believe ZYME represents Canada's Mother Of All Biotechnology (M.O.A.B.) plays amongst the early stage opportunities.

### Analysis

- ◆ **The potential to generate \$5.5 bln from current Big Pharma buy-in.** To date, ZYME has inked deals with six major biopharmaceutical companies: Celgene, GlaxoSmithKline, Eli Lilly, Merck, Daiichi Sankyo, and JNJ. These partnerships in aggregate have the potential to generate \$5.5 bln in non-dilutive milestone payments for the company. We expect new licensing deals in the short term, representing potential catalysts to drive ZYME shares higher.
- ◆ **Expanding wholly owned pipeline with blockbuster potential.** ZYME's lead candidate, ZW25, is a bispecific anti-HER2 antibody which has generated preliminary evidence of anti-tumor efficacy. We believe ZW25 has the potential to become a best-in-class therapeutic, in time competing with Herceptin and Perjeta, two HER2 targeted therapies that generated 2017 sales of \$7.2 bln and \$2.3 bln, respectively. In 2018, we anticipate that ZYME will file an IND for its second clinical asset; a bispecific HER2 targeted antibody drug conjugate. Furthermore, we expect a pipeline reveal of non-HER2 targeting therapeutic candidates within oncology as well as broader therapeutic areas such as autoimmune disease and/or inflammation.
- ◆ **Trading at a 20% discount to IPO.** In May 2017 ZYME raised gross proceeds of \$63.6 mln at \$13.00 per share through its IPO. While we do not believe that a discount alone is a sufficient reason to own a stock, fundamentally the ZYME story has evolved positively since this offering with partner programs advancing, the initiation of a new partnership as well as continued data supporting ZW25 anti-tumor activity. In light of this fundamental progress, we view this pullback as an ideal opportunity to initiate or build upon an existing position at a significant discount to IPO.

### Valuation

Our US\$18.00 target is based on a probability adjusted, net present value, sum-of-the-parts analysis. Specifically, our model attributes \$8.45 of per share value to ZYME's lead clinical asset ZW25, \$1.17 of per share value to ZYME's upcoming follow-on clinical asset ZW49, \$4.80 of per share value from ZYME's strategic partnership and collaboration agreements and \$3.10 of per share value in cash.

GAAP	1Q	2Q	3Q	4Q	Full	Revenues	-
EPS	Mar	Jun	Sep	Dec	Year	(mln)	
2017A	US\$(1.25)	US\$(0.52)	US\$(0.64)	US\$1.79	US\$(0.62)	US\$51,762	
2018E	(0.83)	(0.83)	(0.83)	(0.83)	(3.30)	0	
2019E	(0.96)	(0.96)	(0.96)	(0.96)	(3.83)	0	

Source: Raymond James Ltd., Thomson One

## Table of Contents

Investment Overview.....	3
Company Overview.....	4
Scientific Primer On Antibodies .....	5
Overview Of ZYME’s Therapeutic Platform Technologies.....	6
ZW25: ZYME’s Lead Clinical Candidate .....	15
ZW25: Financial Analysis & Outlook .....	23
ZW49: ZYME’s Near Term Second Clinical Asset.....	26
ZW49: Financial Analysis & Outlook .....	30
Strategic Partnerships and Collaborations.....	33
Valuation & Recommendation .....	35
Appendix A: Financial Statements .....	37
Appendix B: Select Management & Directors .....	40
Risks.....	41

## Investment Overview

### **\$5.5 Bln In Potential Milestones Committed By Big Pharma Partners**

Zymeworks' proprietary platform technologies, which work to optimize the efficacy and safety of protein therapeutics, have garnered significant interest from large global drug developers. To date, ZYME has inked deals with six major biopharmaceutical companies: Celgene, GlaxoSmithKline, Eli Lilly, Merck, Daiichi Sankyo, and Johnson & Johnson. These partnerships in aggregate have the potential to generate \$5.5 bln in non-dilutive developmental, regulatory and sales milestone payments for the company. In time, as partner programs advance deeper into the clinic, we believe ZYME's partnering strategy has the potential to evolve into a revenue annuity model which will aid in the funding of ZYME's proprietary wholly owned pipeline of therapeutic assets. Due to the positive momentum of existing collaborations, we expect that new licensing deals will be announced with both new and existing partners in the short term. These deals would represent potential new catalysts to drive ZYME shares higher.

### **Wholly Owned Pipeline Has Blockbuster Potential**

ZYME's lead drug, ZW25, is a bispecific anti-HER2 antibody which has generated preliminary evidence of anti-tumor efficacy in patients who have progressed through multiple lines of currently approved therapeutics. As of ZYME's most recent data presentation at the San Antonio Breast Cancer conference, ZW25 was associated with a 64% overall disease control rate in 11 evaluable breast cancer patients that had received a median of six prior HER2-targeted treatment regimens. We believe ZW25 has the potential to become a best-in-class therapeutic, competing with the likes of Herceptin and Perjeta, two HER2 targeted therapies that generated 2017 sales of \$7.2 bln and \$2.3 bln, respectively. We expect that ZYME will file an IND for its next clinical candidate, ZW49, an anti-HER2 bispecific antibody drug conjugate in 2018. Furthermore, in 2018 we expect ZYME to unveil a deeper pipeline of non-HER2 targeting therapeutic candidates within oncology as well as broader therapeutic areas such as autoimmune disease and/or inflammation.

### **Trading At A Significant Discount To IPO**

ZYME is currently trading at a ~20% discount to its IPO price in May 2017, which was largely subscribed by existing shareholders (raised gross proceeds of \$63.6 mln at \$13.00 per share). While we do not believe that a discount alone is a sufficient reason to own a stock, we note that fundamentally the Zymeworks story has positively evolved since this offering with partner programs advancing as well as ZW25 continuing to demonstrate durable anti-tumor activity. In light of this fundamental progress, we view this pullback as an ideal opportunity to initiate or build upon an existing position ahead of further ZW25 data releases as well as broader pipeline expansion.

### **Near-Term Catalysts Could Drive Shares Higher**

ZYME recently completed the dose escalation portion of its Phase I study of ZW25. Looking forward, we expect ZYME to release data from the cohort expansion phase of its ZW25 trial at ASCO 2018, which will include multiple cohorts as described within. Beyond ZW25 data, we anticipate that ZYME will file an IND for its second clinical asset, ZW33, an anti-HER2 bispecific antibody drug conjugate in 2018. We expect to gain more granularity around this asset at AACR on April 17, 2018. Finally, we anticipate that ZYME will unveil preclinical data showcasing its broader candidate pipeline and evolving therapeutic platforms this year and further believe that additional near term strategic drug development partnerships are highly probable. Taken together, we view ZYME as an attractive opportunity in the race to produce next-generation, fit for purpose, biotherapeutics.

## Company Overview

### A Platform Technology Company Dedicated To The Discovery, Development and Commercialization of Next-generation Biotherapeutics

Headquartered in Vancouver, British Columbia, Zymeworks Inc. is an innovative, clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization of next-generation multifunctional biotherapeutics. Zymeworks' proprietary technologies include four modular, complementary platforms including the Azymetric, ZymeLink, EFECT and AlbuCORE platforms. The breadth of Zymeworks' wholly owned platform technologies has wide reaching applications across multiple therapeutic areas, and to date has garnered significant interest from the pharmaceutical community culminating in multiple marquee partnerships with leading global drug developers such as Merck, Eli Lilly, Celgene, GlaxoSmithKline, Daiichi Sankyo and most recently, Janssen. In addition to its successes in out-licensing its differentiated expertise and intellectual property, Zymeworks is focused on developing a robust, wholly owned and highly differentiated pipeline of product candidates, with an initial focus in oncology. Zymeworks' current wholly owned product pipeline consists of: I) ZW25, a bispecific antibody directed against human epidermal growth factor receptor 2 (HER2), II) ZW49, a bispecific antibody-drug conjugate (ADC), and III) multiple preclinical and advanced discovery programs. An overview of the company's product candidate pipeline, including partnerships, is presented in Exhibit 1.

#### Exhibit 1: ZYME's Product Candidate Pipeline

Programs	Enabling Platform(s)	Indication(s)	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	WORLDWIDE COMMERCIAL RIGHTS
<b>LEAD PRODUCT CANDIDATES</b>							
ZW25 HER2 x HER2 Bispecific	Azymetric™	Breast, Gastric, & Other HER2-Expressing Cancers	█	█	█		
ZW49 HER2 x HER2 Bispecific ADC	Azymetric™ ZymeLink™	HER2-Expressing Cancers	█	█			
<b>PRECLINICAL AND ADVANCED DISCOVERY PROGRAMS</b>							
Bispecific ADCs	Azymetric™, EFECT™ ZymeLink™	Solid Tumors	█	█			
T Cell Engaging Bispecifics	Azymetric™ EFECT™	Solid Tumors	█	█			
Checkpoint – Modulating Bispecifics	Azymetric™ EFECT™	Solid Tumors	█				
<b>PARTNERSHIPS*</b>							
Bispecific	Azymetric™	Immuno-Oncology	█	█			
Bispecific	Azymetric™, EFECT™	Not Disclosed	█	█			
Bispecific	Azymetric™	Not Disclosed	█	█			
Bispecific	Azymetric™, EFECT™	Not Disclosed	█	█			
Bispecific	Azymetric™, EFECT™	Immuno-Oncology	█	█			
Bispecific	Azymetric™, EFECT™	Not Disclosed	█	█			

Source: Zymeworks Inc.

### Established To Address Shortcomings In Computational Biology

Incorporated in 2003, Zymeworks was created to address a need in the pharmaceutical and chemical markets that was not being adequately serviced by existing protein simulation and engineering approaches. Specifically, at the time, computational biology was dominated by two distinct approaches. The first approach utilized widely distributed open source academic projects, such as the widely popular Folding@home project. While these endeavors have succeeded in elucidating the mechanisms of protein folding, the data lacked commercial relevance and was limited by concerns around stability, modularity and documentation. The second widely utilized approach involved in silico platforms designed for very specific purposes, such as SIFT and PolyPhen, two platforms designed to predict the functional impact of amino acid substitutions on the structure and function of a human protein. While these discrete algorithms afforded more functional relevance from a clinical or commercial perspective, these platforms failed to capture recent advances in protein biochemistry or computing architecture.

In response to an ongoing commercial need for a comprehensive, flexible and evolving platform for in silico protein modeling and engineering, Zymeworks developed its ZymeCAD engine, which would become the foundation for a number of Zymeworks' therapeutic platforms. Initial validation of the ZymeCAD engine came through Zymeworks' first research collaboration with Weyerhaeuser in 2005. Under the Weyerhaeuser collaboration, Zymeworks was tasked with researching enzymes that would make pulp and paper processing more efficient and eco-friendly. Following the Weyerhaeuser deal, Zymeworks' predictive protein engineering tools continued to garner interest and ultimately led to the company's second deal, with Royal DSM N.V. to evaluate new enzymes for use in DSM's biocatalytical processes. Clearly, Zymeworks technology was succeeding where others were not, which is why in 2007, the company undertook a strategic shift, focusing its protein modeling and engineering expertise onto antibody therapeutics, a lucrative and meaningful area in need of better predictive technologies. Therapeutics is where the company remains firmly focused today.

## Scientific Primer On Antibodies

### Antibody Therapeutics Are Among The Fastest Growing Biopharmaceuticals

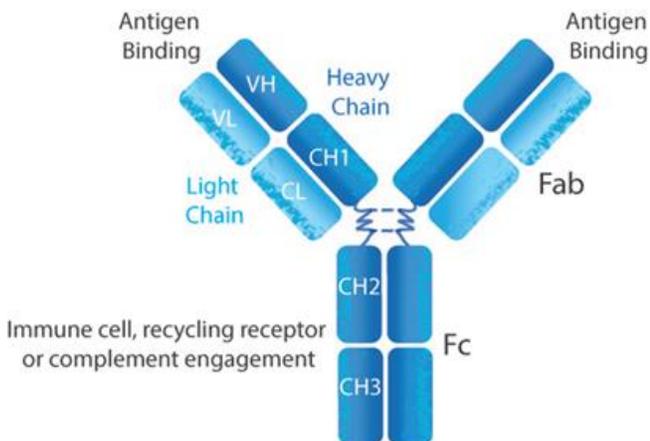
Antibody based therapeutics are among the fastest growing biopharmaceuticals, fueled by intensive research and huge capital investment aimed at generating novel therapeutics with blockbuster clinical and commercial value. Since the approval of the first monoclonal antibody rituximab in 1986 (muromonab-CD3 marketed by Janssen) more than 75 antibody-based molecules have been approved by a regulatory authority in a major pharmaceutical market. Interestingly, with specific reference to oncology, the three largest-selling oncology therapeutics are monoclonal antibodies; Rituxan, Herceptin, and Avastin which generated 2017 worldwide sales of approximately \$7.7 bln, \$7.2 bln and \$6.9 bln, respectively. Currently, there are over 300 monoclonal antibodies in various stages of clinical development with combined global sales expected to reach approximately \$125 bln. In order to appreciate the value of antibody-based therapeutic development, we believe a quick "scientific" primer on antibody biology is warranted.

### Antibodies Are The "Scouts" Of The Immune System

Antibodies, also known as immunoglobulins, are Y-shaped proteins that are produced by the immune system to help neutralize specific targets, or antigens. Antigens can be anything from viruses, bacteria, other cells or molecules. One can think of an antibody as the "scout" of the immune system. They find antigens, attach to them and flag them to the immune system.

Antibodies are produced by B cells of the immune system and typical monoclonal antibodies are symmetrical molecules consisting of four peptide chains, including two heavy chains and two identical light chains (see Exhibit 2).

#### Exhibit 2: Typical Monoclonal Antibody



Source: Zymeworks Inc.

In the exhibit above, the tips of the “Y” shape are denoted Fab and the base of the “Y” is denoted the Fc region. The tips contain a paratope (think of a lock) that is specific for one particular epitope (think of a key) on an antigen, allowing these two structures to bind together with high precision. As a result of the symmetrical nature of an antibody’s arms, an antibody can engage two copies of its target antigen simultaneously. The ability of an antibody to communicate with the other components of the immune system is mediated via its Fc region.

Despite the success of monoclonal antibody therapeutics, these therapies are not without their limitations. For example, the majority of patients who initially respond to monoclonal antibody therapy eventually relapse due to acquired resistance through spontaneous mutation, or due to extensive cross-talk among some signaling pathways. In an attempt to overcome the shortcomings of monoclonal antibody therapy and improve the treatment effectiveness of antibody based therapies, bispecific antibodies have garnered significant interest.

### **Bispecific Antibodies Bind Two Different Epitopes**

Bispecific antibodies, also termed “dual targeting” or “dual specificity” antibodies have the ability to bind two different targets on the same, or different, cells. These targets may be cell surface receptors or even soluble ligands. These dual-nature antibodies have key advantages that can potentially enhance therapeutic efficacy compared with monotherapy, or traditional combination therapies, by:

- 1) Simultaneously blocking two different targets or mediators that have a primary role in the disease pathogenesis
- 2) Inducing cell signaling pathways
- 3) Retargeting to mediate antibody-dependent cell mediated cytotoxicity (ADCC)
- 4) Avoiding the development of resistance and increasing antiproliferative effects
- 5) Temporarily engaging a patient’s own immune cells (such as T cells, macrophages, NK cells) to target cancer cells, thus activating cytotoxic T cells to cause tumor lysis (or other mechanisms of cellular mediated cytotoxicity)

Bispecific antibodies are now one of the fastest-growing classes of investigational drugs. In addition to the approved cancer bispecifics, blinatumab (Blinicyto, Amgen) and catumaxomab (Removab, Fresenius Biotech), there are currently greater than 50 bispecifics in clinical development, the majority focused on oncology indications. While there is a diverse ecosystem of bispecific antibody formats which are beyond the scope of this report, we believe that Zymeworks has developed one of the most versatile toolboxes offering them exceptional flexibility in their development endeavors through their multiple platform technologies.

## **Overview Of ZYME’s Therapeutic Platform Technologies**

### **We Believe Next-Generation Targeted Therapeutics Will Be Multifunctional**

With respect to cancer, targeted therapeutics are small molecule or biologic substances that block the replication and propagation of cancer by interfering with specific molecular targets. Targeted therapies differ from chemotherapies in a number of ways. For example:

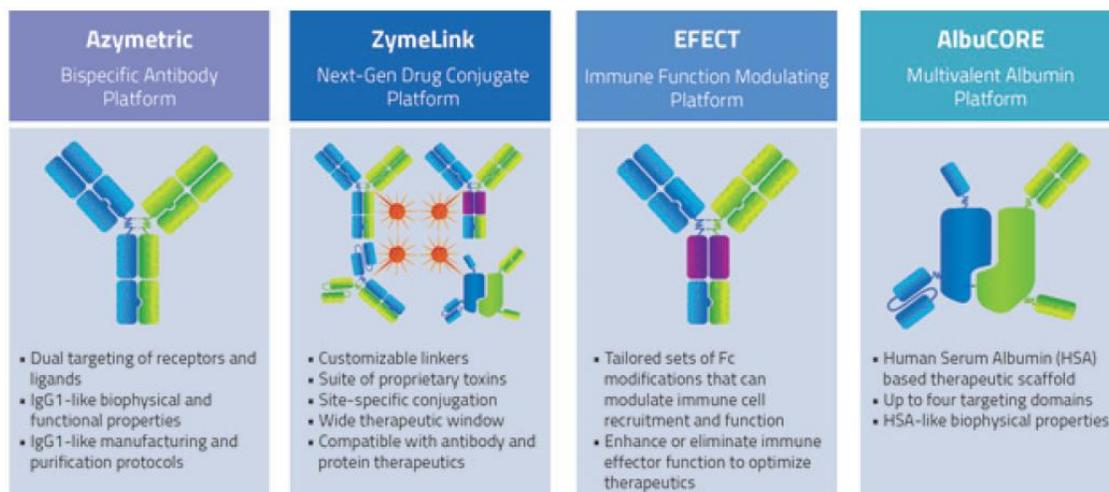
- I. Targeted therapies act on specific molecular targets associated with the carcinoma, whereas most standard chemotherapies act on all rapidly dividing normal and cancerous cells
- II. Targeted therapies are rationally chosen to interact with a specific target, whereas many standard chemotherapies were identified simply due to their cytotoxic effect (i.e. they kill normal cells)

- III. Targeted therapies can be both cytostatic and cytotoxic (i.e. they block tumor cell proliferation and may induce apoptosis or senescence), whereas standard chemotherapy agents are typically only cytotoxic (i.e. they kill all cells).

As a result of these differentiating aspects, targeted therapies have led to significant improvements in patient outcomes when compared to chemotherapies; however, they are not without their limitations. For example, some cancer patients acquire resistance, become refractory to, or cannot tolerate the increased toxicity of these treatments. Furthermore, many of these treatments often only delay disease progression and do not induce a durable cancer remission. Clearly, there is a need for new next-generation targeted therapies with improved, long-lasting efficacy and reduced toxicity. In our view, this next generation will be punctuated by multifunctional therapeutics specifically designed to act through several synergistic mechanisms of action to enhance efficacy, overcome resistance and minimize side effects.

ZYME's expertise in protein engineering has enabled the development of a number of proprietary platform technologies which can be utilized in the development of next generation, targeted therapeutics. ZYME's platforms can be used alone or in combination with a synergistic effect to develop fit-for-purpose biotherapeutics with bispecific capabilities (Azymetric), cytotoxic payload delivery (ZymeLink), finely tuned immune cell regulation (EFECT) and multivalent targeting (AlbuCORE).

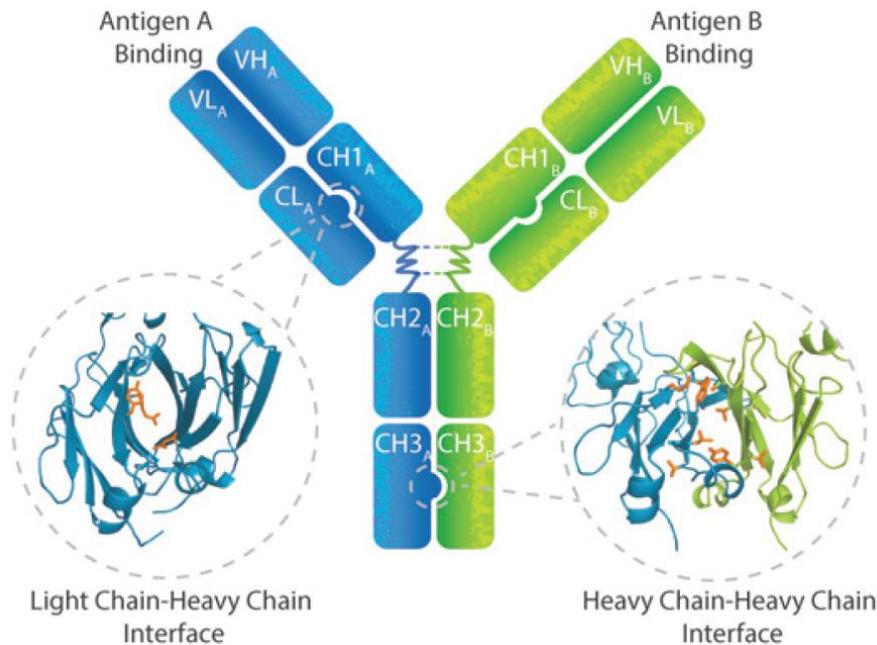
### Exhibit 3: ZYME's Proprietary Therapeutic Platforms



Source: Zymeworks Inc.

### Azymetric: Bispecific Antibody Platform

Azymetric bispecific antibodies consist of two different heavy chains and two different light chains which when assembled can bind to two distinct antigens, or epitopes, via its two unique antigen targeting arms. The underlying technology of the Azymetric platform involves a library of proprietary amino acid substitutions in the Fc and Fab regions that transforms monospecific antibodies into bispecific antibodies. Specifically, complementary amino acid substitutions on each of the CH3 domains, engineered by ZYME, facilitate the interaction of two distinct heavy chains while inhibiting the interaction of two identical heavy chains. Furthermore, additional amino acid substitutions are introduced at the heavy-light chain interfaces which mediates the correct pairing of the heavy chains with their respective light chains (see Exhibit 4).

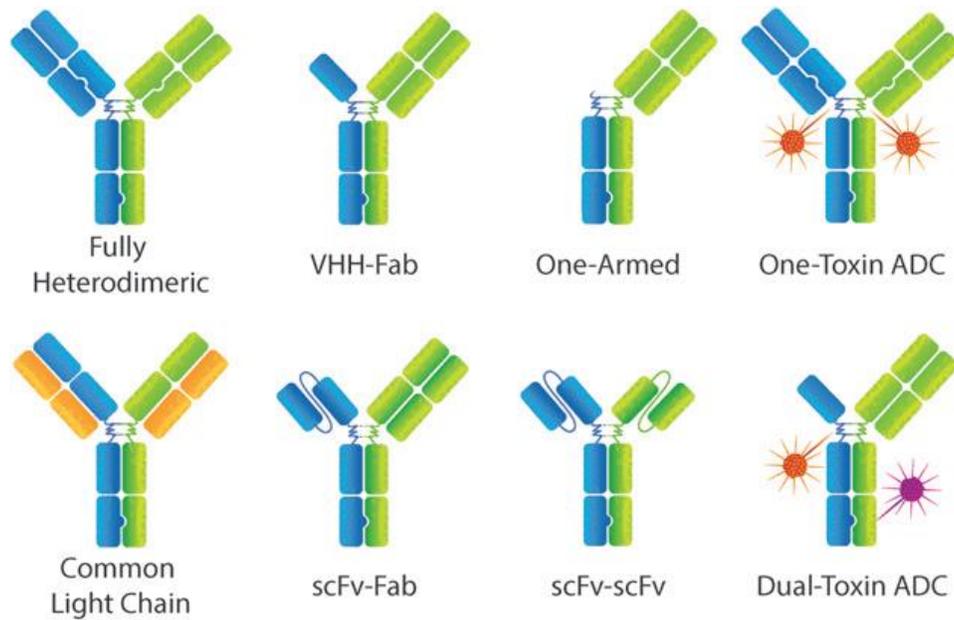
**Exhibit 4: Azymetric Bispecific Antibody Platform**

Source: Zymeworks Inc.

While there are a number of competing bispecific technologies, many of these technologies are hindered by poor stability resulting from significant alteration of the native antibody structure, toxicity issues and complex manufacturing processes. Zymeworks' elegant solution to these persistent issues is to simply retain the desirable features of naturally occurring monoclonal IgG antibodies, such as their low immunogenicity, long serum half-life, high stability and the ability to mediate effector function. Furthermore, Azymetric antibodies are manufactured using industry-standard monoclonal antibody processes which enables high production yields and product purity. The end result of the Azymetric platform is a "plug-and-play", low cost, high quality manufacturing process for both ZYME's proprietary and partnered product candidates.

Another key differentiating factor between Azymetric and other competing bispecific platforms is that the Azymetric platform is compatible with alternative antigen binding formats including Fab fragments and single chain antibodies. ZYME believes that this unique flexibility enables it to rapidly explore multiple different structural variants and to select the format that provides optimized engagement geometry for a given target to maximize therapeutic effect. As drug developers continue to elucidate highly complex pathogenic processes, such as carcinogenesis, we share ZYME's view that it is this level of therapeutic customization that will be required to design efficacious next-generation therapeutics.

### Exhibit 5: Azymetric Bispecific Antibody Format Variants



Source: Zymeworks Inc.

Zymeworks' wholly owned, lead clinical candidates, ZW25 and ZW49 (soon to be clinical), which we discuss below, are based upon the Azymetric platform. To date, ZYME has licensed the Azymetric platform to Merck, Eli Lilly, Celgene, GlaxoSmithKline, Daiichi Sankyo and Janssen for the development of their own targeted therapeutics.

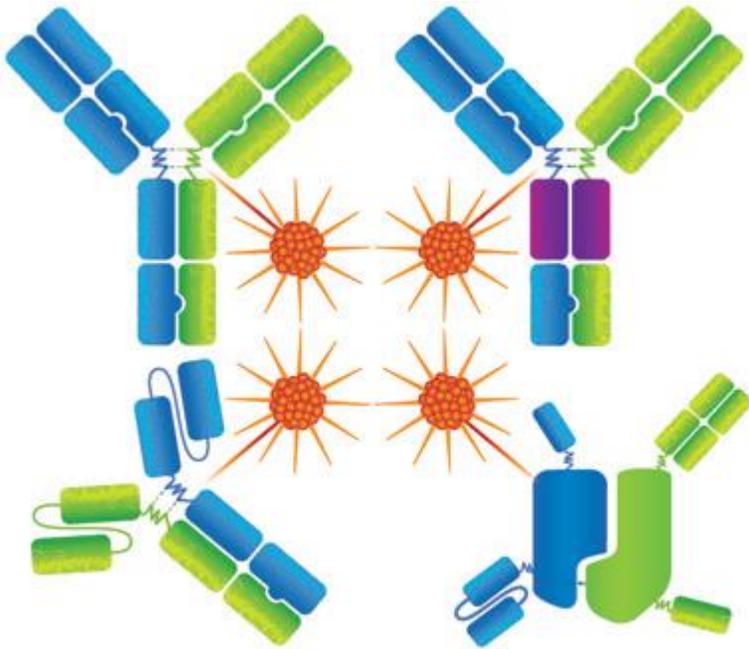
### ZymeLink: Antibody Drug Conjugate Platform

On December 21, 2015, ZYME acquired a 19.99% ownership interest in Kairos, a privately held company specializing in the discovery and development of antibody-drug conjugates (ADCs) for \$3.6 mln cash. On March 18, 2016, ZYME completed the acquisition of the remaining shares of Kairos for \$24.8 mln, comprising \$23.0 mln in common share equity of ZYME (1,822,656 shares issued in total) and \$1.7 mln in cash. The acquisition gave Zymeworks full ownership over the Kairos technology which formed the basis for the ZymeLink platform.

Today, the ZymeLink conjugation platform represents a suite of novel site-specific protein conjugation technologies and customizable cleavable linkers that enable the delivery of cytotoxic payloads. The ZymeLink suite of tools can be applied to all of Zymeworks' antibody and albumin-based therapeutic scaffolds. The platform enables the production of homogeneous product candidates that are stable in circulation but will efficiently release the conjugated payload upon internalization by target cells.

For antibodies, the ZymeLink platform has been specifically engineered to preserve Fc effector function to facilitate the recruitment and activation of immune cells as well as to maintain typical antibody pharmacokinetics. ZYME believes by maintaining this structural integrity it should be able to reduce off-target effects and thus improve tolerability.

### Exhibit 6: ZymeLink Drug Conjugate Platform

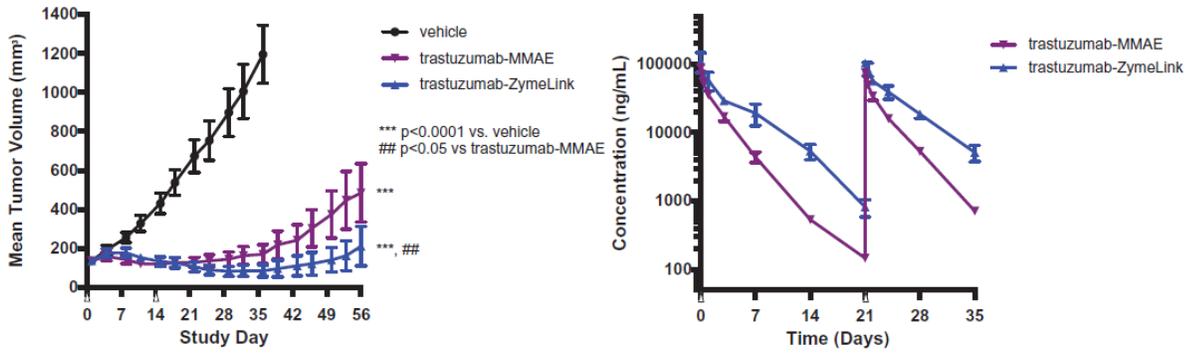


Source: Zymeworks Inc.

In addition to its protein conjugation technologies, ZYME has developed a series of proprietary cytotoxic payloads, spanning multiple classes, which possess highly potent anti-tumor activity against a diverse range of cancer cell types. Notably, ZYME's conjugation platform is compatible with a variety of small molecule therapeutics other than Zymeworks' proprietary cytotoxic payloads. Furthermore, ZymeLink is compatible with multiple antibody and protein formats including Azymetric, AlbuCORE and other traditional monoclonal antibody formats.

ZymeLink-cytotoxin conjugates have demonstrated impressive anti-tumor activity and tolerability *in vivo* in preclinical studies. For example, as demonstrated in the left panel of Exhibit 7, an ADC generated using the ZymeLink platform demonstrated greater potency than an ADC generated via the MMAE (monomethyl auristatin E) platform. Specifically, the study utilized a HER2-expressing patient derived breast cancer model, where either trastuzumab-ZymeLink or Trastuzumab-MMAE were administered to xenograft mice (n=9 mice/group) at 3mg/kg on day 0 and day 14. Treatment with trastuzumab-ZymeLink inhibited the relative growth rate of tumors when compared to trastuzumab-MMAE, and the results were statistically significant ( $p < 0.005$ ).

**Exhibit 7: ZymeLink Antibody-Drug Conjugates Are Superior To MMAE Conjugates**



Primate Safety	Trastuzumab-MMAE	Trastuzumab-ZymeLink
Dose-limiting Toxicity	Myelotoxicity (6 mg/kg)	Elevated AST/ALT (24 mg/kg)
Maximum Tolerated Dose	3 mg/kg	18 mg/kg

Source: Zymeworks Inc.

Tolerability of the ZymeLink ADC was also assessed relative to the MMAE ADC in a four-week non-human primate tolerability study (the right panel of Exhibit 7). In this study, the maximum tolerated dose (MTD) of the ZymeLink ADC was 18 mg/kg based on elevated levels of AST and ALT at 24 mg/kg. The MTD for the MMAE ADC was determined to be 3mg/kg based on severe myelotoxicity at 6 mg/kg. Most interestingly is that, at equivalent doses, the ZymeLink ADC had greater drug exposure than the MMAE ADC implying a much larger therapeutic window for the ZymeLink ADC.

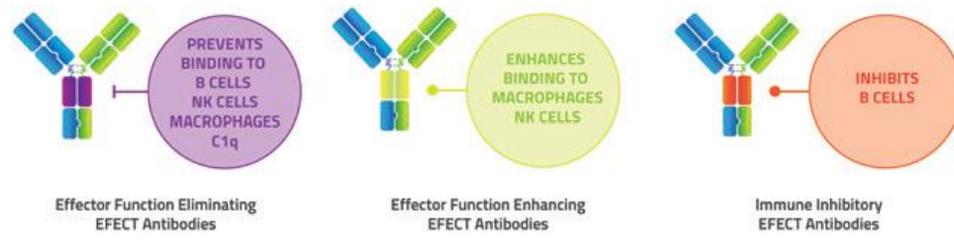
Zymeworks has not yet partnered the ZymeLink platform and all assets utilizing the technology are currently preclinical.

**EFECT: Antibody Effector Function Modulation Platform**

Immune cells bind to the Fc region of antibodies through proteins called Fc receptors. When bound, some Fc receptors activate immune cell function while others inhibit immune cell function. Whether Fc signaling is activating or inhibitory depends on the isoform of the Fc receptor expressed by the immune cell (FcγRIIIa and FcγRIIIa activate while FcγRIIb inhibit).

The Effector Function Enhancement and Control Technology (EFECT) platform comprises a library of Fc modifications that can selectively modulate the activity of recruited immune cells including upregulation to enhance antibody-mediated effector cytotoxicity, and downregulation to suppress unwanted effector activity for certain therapeutic applications. Specifically, EFECT platform modifications can be introduced into the Fc region of antibodies to generate therapeutics with three different functional outcomes: i) immune effector function elimination (“Effector Function Eliminating”), ii) enhanced immune effector function (“Effector Function Enhancing”), or iii) the ability to inhibit B cell activity without depleting B cells (“Immune Inhibitory”). These functional outcomes are illustrated in Exhibit 8.

### Exhibit 8: Modulation of Effector Function With The EFECT Platform



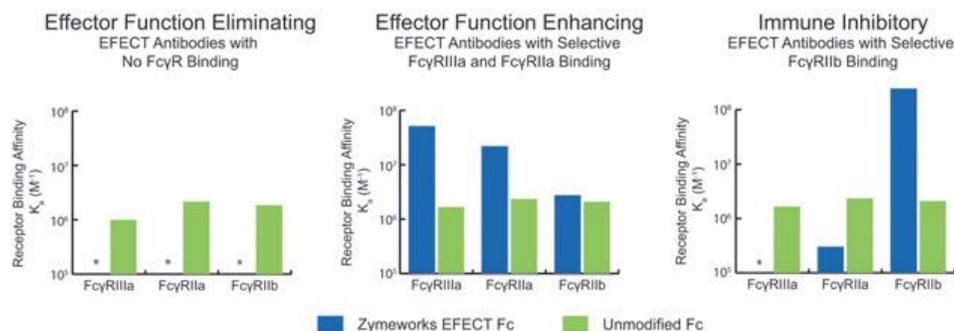
Source: Zymeworks Inc.

Zymeworks is able to modulate the activity of recruited immune cells by introducing proprietary mutations to the CH2 domain of the antibody's Fc to selectively modulate an antibody's interaction with Fc-gamma receptors (FcγR) expressed on the surface of immune cells and with components of the complement pathway.

EFECT variants that have selectively increased binding to the FcγRIIIa and/or FcγRIIIa receptors display enhanced ADCC (NK-cell driven), ADCP (macrophage driven) and serum clearance of immune complexes.

EFECT variants with enhanced binding to FcγRIIb can inhibit antibody-mediated auto-immunity by downregulating immune responses of B cells, permitting antibody cross-linking through immune cell engagement without immune cell activation.

### Exhibit 9: Fc Receptor Binding Affinity – EFECT Fc Vs. Unmodified Fc



Source: Zymeworks Inc.

By upregulating, downregulating or eliminating immune cell engagement, the EFECT platform enables Zymeworks the ability to tailor a product candidate's effector function to produce the precisely desired therapeutic effect. For example, for the development of T cell redirecting bispecific antibodies, using the Effector Function Eliminating modifications prevents binding between the antibody's Fc region and the Fc receptors of immune cells, which may otherwise lead to inadvertent toxicity. Furthermore, for more traditional anti-cancer therapeutic antibodies, using the Effector Function Enhancing modifications improves binding between the antibody's Fc region and activating Fc receptors, which may enhance immune cell-mediated anti-cancer activity.

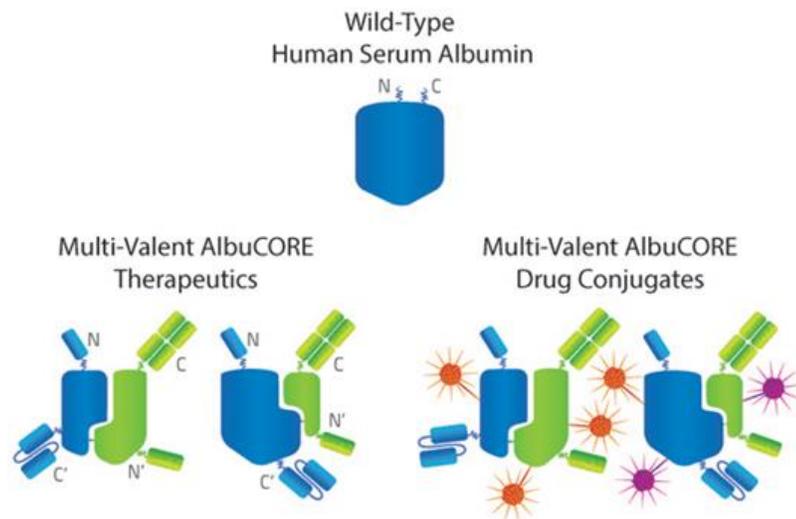
The EFECT platform is compatible with both traditional monospecific antibodies and Zymeworks' Azymetric bispecific antibodies. To date, ZYME has licensed certain aspects of this platform to Merck, GSK, Daiichi and JNJ for use in conjunction with the Azymetric platform. ZYME has also entered into a collaboration with GSK for the further development and commercialization of the EFECT platform. Currently, all ZYME wholly owned pipeline products based on the EFECT platform are preclinical.

## AlbuCORE: Multispecific Antibody Alternative Platform

AlbuCORE was developed as a flexible, alternative platform to antibodies where it is advantageous for a multi-valent therapeutic to target multiple disease targets. AlbuCORE achieves multispecificity by utilizing a proprietary suite of multivalent scaffolds engineered from the human serum albumin (HSA) protein. This platform is highly flexible and enables the addition of up to four customizable targeting domains, which allows for additional tumor specificity and synergistic activity as well as increased affinity and selectivity for the desired target. The resulting superstructure naturally accumulates in tumor microenvironments or areas of inflammation and benefits from several attractive attributes of HSA, including superior pharmacokinetics and stability. Furthermore, the AlbuCORE constructs possess standard manufacturing and purification protocols compatible with industry standard conjugation technologies which accelerate development and reduce manufacturing costs.

Engineered AlbuCORE is heterodimeric (meaning it is a protein comprising two polypeptide chains differing in composition) and presents two amino termini and two carboxyl termini. To achieve this structure, ZYME evaluated a number of positions where the wildtype HSA amino acid sequence could be split into two polypeptide chains. When the two separate chains are co-expressed, they efficiently and spontaneously associate to reform a native-like HSA structure with four available termini to which antigen-targeting domains can be fused, or other agents chemically conjugated.

### Exhibit 10: AlbuCORE Platform Schematic

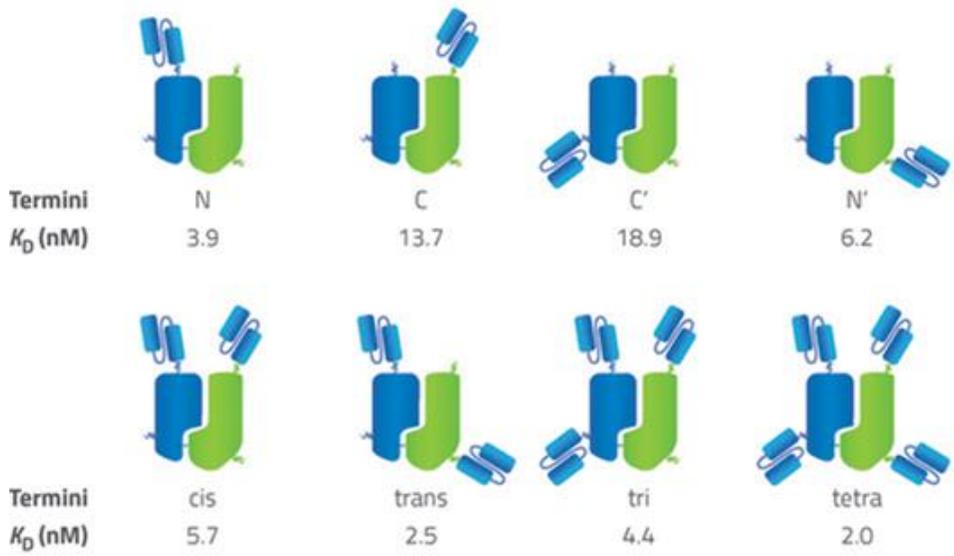


Source: Zymeworks Inc.

Product candidates generated utilizing the AlbuCORE platform retain the features of HSA as a therapeutic scaffold. AlbuCORE variants exploit the natural accumulation of albumin in tumors through enhanced tumor permeability and retention, and the increased demand by tumors for albumin as a source of energy and amino acids. AlbuCORE variants retain the pharmacokinetic properties of HSA, which have previously been exploited by fusing HSA to peptides, hormones and cytokines to extend the half-life of these otherwise rapidly cleared molecules. Unlike antibodies, AlbuCORE-based biotherapeutics inherently lack effector function, which may be desirable in certain therapeutic designs.

From a manufacturing perspective, AlbuCORE variants retain the stability and solubility characteristics of native HSA and thus can be produced in microbial expression systems at a significantly reduced cost relative to other systems.

AlbuCORE's multivalent binding capabilities enable ZYME to design therapeutics with high binding affinity and diverse flexibility. Similar to the Azymetric platform, the AlbuCORE platform also offers the flexibility to test multiple formats with variable inter-termini distances and geometries. This enables ZYME to identify variants with the optimal targeting geometries needed to induce maximal therapeutic effect.

**Exhibit 11: AlbuCORE binding affinity ( $K_D$ ) And Diverse Scaffold Geometries**

Source: Zymeworks Inc.

Zymeworks has not yet partnered the AlbuCORE platform and all assets utilizing the technology are currently preclinical.

**ZymeCAD: The Unifying Computational Backbone**

All of ZYME's therapeutic platforms are enabled by its protein engineering expertise and by utilizing its proprietary computational modeling technology, ZymeCAD. In short, ZymeCAD is a constantly evolving, comprehensive approach to predictive protein modeling and structure-guided protein engineering. ZYME utilizes this software suite to develop better therapeutic platforms by modeling out structure-function relationships and generating predictive biophysical characteristics of specific protein changes. Currently, the ZymeCAD software modules include:

**Molecular Modeling:** A number of proprietary software tools are used to build and refine the quality of high-definition molecular models, incorporating structural data from multiple sources including crystallography, homology and sequence data as well as experimentally derived data.

**Conformational Dynamics:** A number of simulation approaches are utilized to sample and evaluate changes within molecular systems, including protein backbone, sidechain and interdomain changes. These simulations provide ZYME with an understanding of the alternate states and functional characteristics of the protein of interest, including target binding and stability.

**Hot Spot Determination:** Various algorithms are utilized to determine, *in silico*, the specific subset of amino acids in a protein that is critical to determining its functional characteristic and overall stability. This knowledge is critical in elucidating the downstream impact of altering specific hot spots and thus can help drive the rational design and engineering of product candidates.

**Energy Function and Scoring:** Proprietary energy and scoring functions help rank the stability of proteins and binding energies across protein-target interfaces, and the outward-facing surfaces of the proteins.

Overall, it is ZYME's unique software engineering practices that enable the company's rational design and risk mitigated selection of therapeutic candidates.

## ZW25: ZYME's Lead Clinical Candidate

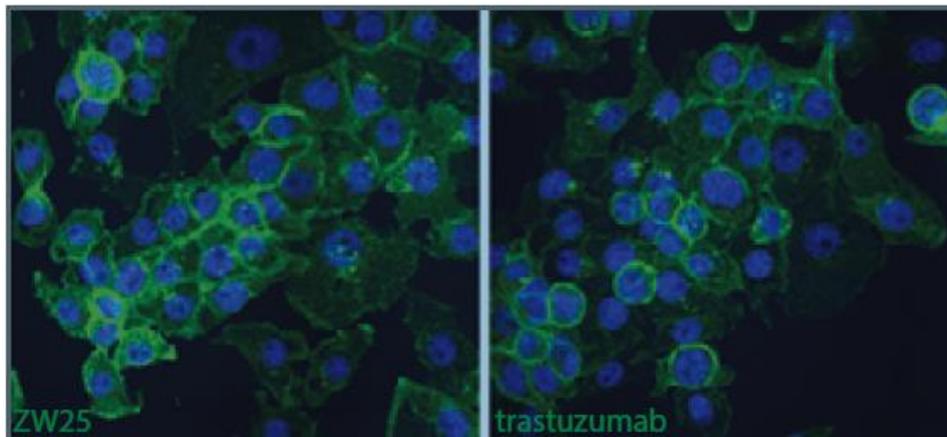
### ZW25: A Biparatopic, Bispecific, Asymmetric Antibody

Developed utilizing the Asymmetric platform, ZW25 is Zymeworks' lead clinical product candidate currently being evaluated in an adaptive Phase I clinical trial in the US. ZW25 is a bispecific antibody that can simultaneously bind two non-overlapping epitopes (biparatopic binding) of HER2. ZW25 binds to the same extracellular domains of HER2 as trastuzumab (Herceptin) and pertuzumab (Perjeta), two blockbuster HER2+ breast cancer therapeutics which generated 2017 sales of \$7.2 bln (+6% Y/Y) and \$2.3 bln (+28% Y/Y), respectively.

Relative to competing HER2 targeted therapies, ZW25's biparatopic binding results in dual HER2 signal blockage, increased binding and removal of HER2 protein from the cell surface and potent effector function. As such, ZW25 has demonstrated increased binding and internalization compared to Herceptin alone (see Exhibit 12). It is this unique feature of ZW25 that has resulted in the asset demonstrating impressive anti-tumor activity in preclinical models of breast cancer, including activity in Herceptin-resistant tumors as well as in tumors with lower levels of HER2 expression. Importantly, approximately 81% of patients with HER2-expressing breast cancer and 57% of patients with HER2-expressing gastric and gastroesophageal junction cancer have tumors that express low to intermediate levels of HER2, making them ineligible for treatment with currently approved HER2-targeted therapies. Therefore, there is a clear significant unmet medical need for HER2-targeted therapeutics that can effectively treat these patient populations.

ZW25 is being developed as a potentially best-in-class HER2 targeted antibody intended as a treatment option for patients with any solid tumor that expresses HER2. ZYME's initial focus is on the treatment of patients with breast or gastric cancers who have progressed after treatment with HER2-targeted therapies or who are not eligible for approved HER2-targeted therapies based on low to intermediate levels of HER2 expression. Pending data, ZYME may expand ZW25 into other HER2-expressing cancer indications, including ovarian cancer. In ZYME's Phase I trial, ZW25 has already demonstrated preliminary anti-tumor activity in patients who have progressed after several lines of treatment. ZW25 has been granted Orphan Drug Designation for the treatment of both gastric and ovarian cancer in the US.

#### Exhibit 12: ZW25 Demonstrates Superior Binding Compared To Trastuzumab



Source: Zymeworks Inc.

### HER2: A Well Validated Target

HER2 is a member of the HER family of receptors. These receptors play a central role in the pathogenesis of several human cancers. They regulate cell growth, survival, and differentiation via multiple transduction pathways and participate in cellular proliferation and differentiation. The family is made up of four main members: HER1, HER2, HER3 and HER4. All four receptors comprise a cysteine-rich extracellular ligand binding site, a transmembrane lipophilic segment, and an intracellular domain with tyrosine kinase catalytic activity.

HER2 was discovered by a group of scientists at MIT and Harvard University. It is a 1255 amino acid, 185 kD transmembrane glycoprotein located at the long arm of chromosome 17. HER2 is expressed in multiple tissues and its major role in those tissues is to facilitate excessive/uncontrolled cell growth and tumorigenesis. In cancerous cells the HER2 gene can, and in many cases is, amplified. The resulting amplification of HER2 increases the number of HER2 receptors that are expressed on the cell surface which in turn results in dysregulated cell signaling which can accelerate cell growth, inhibit apoptosis and increase cell motility, propagating carcinogenesis.

Amplification of HER2 occurs in approximately 15-25% of breast cancers and 10-30% of gastric/esophageal cancers, amongst others (see Exhibit 13).

#### **Exhibit 13: Incidence Of HER2 Gene Expression In Various Cancers**

<b>Cancer Type</b>	<b>Incidence of High HER2 Expression</b>
Breast . . . . .	~20%
Bladder . . . . .	5-15%
Endometrial . . . . .	8-35%
Ovarian . . . . .	6.7%
Gastroesophageal . . . . .	4-22%
Pancreatic . . . . .	2-29%
Cervical . . . . .	1-21%
Head & Neck . . . . .	3%
Colorectal . . . . .	2-3%
Lung . . . . .	1-6%
Melanoma . . . . .	0-5%

Source: Yan et al., 2014, Zymeworks Inc.

HER2 expression thus serves as both a prognostic and predictive biomarker and has been a particularly effective target for breast and gastric cancer treatment. Specifically, the level of HER2 expression has become an important biomarker to help guide clinical decisions in the context of HER2 targeted therapies. Typically, HER2 protein expression is screened by immunohistochemistry and is assigned a value from 0 (baseline expression) to 3+ (extraordinarily high expression). HER2 gene amplification can similarly be determined via fluorescence in situ hybridization (FISH), and scored as either negative (two copies) or positive (greater than 2 copies). The HER2 expression status of a cancer can be characterized as High, Intermediate, Low or Negative as per the following table:

**Exhibit 14: Cancer Characterized by HER2 Status**

Cancer Classification According to HER2 Status

		IHC				FISH			HER2-Targeted Therapies	
		3+	2+	1+	0	Positive	Equivocal	Negative	Approved	Zymeworks Candidates
HER2 Expression Classification	HER2 High	X							Herceptin, Perjeta, Kadcyla, Tykerb	ZW25 ZW33
	HER2 Intermediate		X			X		X	None	ZW25 ZW33
	HER2 Low			X			X	X	None	ZW25 ZW33
	HER2 Negative				X			X	N/A	N/A

Source: Zymeworks Inc.

While any level of HER2 expression can impact tumor growth and survival, current HER2 targeted therapies have only demonstrated efficacy in breast and gastric cancers with the highest levels of HER2 expression. As such, there remains a significant need for targeted therapies that could prove effective at lower levels of expression. We believe ZYME is exceptionally well positioned to develop such a targeted therapy either with ZW25 or ZW49.

### Anti-HER2 Therapies Have Significantly Altered The Treatment Paradigm In HER2+ Breast Cancer

Breast Cancer (BrCa) is the most commonly diagnosed cancer worldwide. Approximately 1 in 8 women in the US will develop invasive BrCa over the course of her lifetime. In 2017, an estimated 252,710 new cases of invasive BrCa are expected to be diagnosed in the US and approximately 40,610 women are expected to die. As of March 2017, the prevalence of BrCa in the US was estimated to be approximately 3.1 mln.

High HER2 expression accounts for approximately 20% of breast cancers. In breast cancer, disease stage, grade, HER2 and hormone status remain the only predictive factors for the selection of targeted therapies. Other molecular markers, such as mutations in PIK3CA or PTEN, have been assessed to further select a group of patients who could benefit from anti-HER2 therapy, especially from the dual blockage approach; however, this has yet to enter routine clinical practice. To date, five drugs targeting HER2 have been approved by the FDA for the treatment of early and late stage BrCas that overexpress HER2; we review those therapeutics in Exhibit 15.

### Exhibit 15: Commercial HER2 Targeting BrCa Therapeutics

Therapeutic	Class	Mechanism of Action	Indication
<i>Trastuzumab</i>	Monoclonal antibody	Inhibits ligand-independent HER2 and HER3 signalling, inhibits the shedding from the extracellular domain and might trigger antibody-dependant cellular cytotoxicity	HER2+ early BrCa, HER2+ mBrCa
<i>Lapatinib</i>	Tyrosine kinase inhibitor	Dual inhibitor of HER2	HER2+ mBrCa in combo with capecitabine, trastuzumab, or an aromatase inhibitor
<i>Pertuzumab</i>	Monoclonal antibody	Directed at the dimerisation domain of HER2	HER2+ mBrCa that has not been treated with chemo, or together with trastuzumab and docetaxel for non-operable HER2+ BrCa
<i>Trastuzumab emtansine</i>	Antibody-drug conjugate	Trastuzumab is stably linked to a potent microtubule inhibitor that is a derivative of maytansine	HER2+ advanced or mBrCa in adults who previously received trastuzumab and taxane
<i>Neratinib</i>	Tyrosine kinase inhibitor	Inhibitor of HER1, HER2 and HER4	Extended adjuvant treatment of early stage, HER2+ BrCa

Source: Loibl et al, 2016, Raymond James Ltd.

Current standard of care for HER2 high BrCa is built on a backbone of HER2 inhibition throughout all lines of therapy. For metastatic disease (mBrCa), first line standard of care therapy consists of Herceptin (trastuzumab), Perjeta (pertuzumab) and a taxane. The efficacy of this dual blockade was demonstrated in the CLEOPATRA trial, in which median overall survival was demonstrated to be 56.5 months, an extension over 40 months in the control group which received trastuzumab and a placebo (in addition to docetaxel).

Second line standard of care is Kadcyla. In the EMILIA study, treatment with Kadcyla was associated with a median progression free survival (PFS) of 0.6 months and a median overall survival of 30.9 months vs. a median overall survival of 25.1 months for the combination of Tykerb and capecitabine. For patients who have progressed beyond Herceptin, Perjeta and Kadcyla, there is no preferred treatment. Options for these patients involve Herceptin plus chemotherapy, Herceptin plus Tykerb or Tykerb plus Xeloda. These regimens are generally associated with a median PFS of less than four months. While HER2 targeted therapies are effective in many patients with HER2 high BrCa, some patients fail to respond to these drugs and all patients with metastatic disease ultimately relapse.

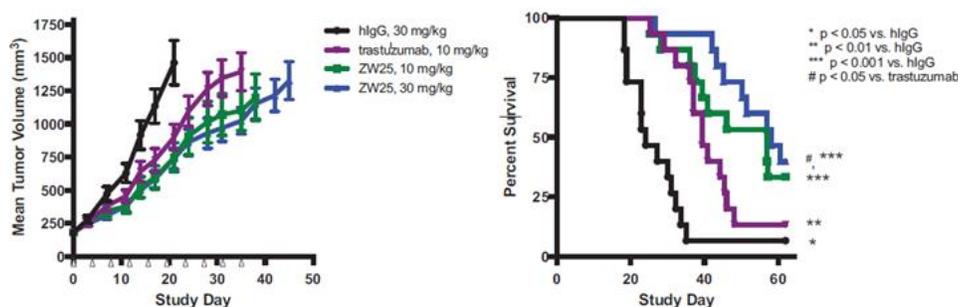
In addition to improved options for HER2 high breast cancer, there is a need for HER2-targeted therapies that can effectively treat cancers with lower levels of HER2 expression. Approximately 81% of patients with HER2-expressing breast cancer have tumors that express low to intermediate levels of HER2. Currently approved HER2-targeted therapies, such as Herceptin and Perjeta, are not sufficiently active to provide clinical benefit to these patients. Some of these patients may have tumors that express either or both the estrogen receptor and progesterone receptor and may receive hormone therapies such as tamoxifen, which can result in an average overall survival benefit of 43.3 months. However, tumors that lack expression of the estrogen and progesterone receptors and express HER2 at low to intermediate levels are currently classified as triple negative. These patients receive cytotoxic chemotherapy and generally have a far poorer prognosis, living 13.3 months, on average. ZYME believes replacing or adding ZW25 to the existing standard of care for these molecular subtypes will lead to improved survival for these patients.

### ZW25 Preclinical Efficacy In HER2 Low To Intermediate BrCa

In multiple preclinical studies, ZYME has demonstrated that ZW25 confers anti-tumor activity against breast tumors expressing low to intermediate levels of HER2 as well as ovarian cancer. Neither Herceptin nor Perjeta have been approved for use in these settings. ZYME's preclinical data also supports the potential for superiority of ZW25 over Herceptin in gastric cancer, where ZW25 demonstrated complete responses in a patient-derived gastric tumor model.

Starting off with BrCa, ZYME has demonstrated that ZW25 is effective in a HER2 low BrCa patient-derived xenograft model. In this study, mice with established tumors were administered antibody therapy twice weekly for five weeks in a blinded, randomized placebo controlled fashion (n=15 mice/group). As shown in Exhibit 16, ZW25 at both 10 mg/kg and 30 mg/kg, inhibited tumor growth and prolonged survival compared with control IgG (p<0.001). Furthermore, ZW25 at 30 mg/kg significantly prolonged survival over Herceptin at 10 mg/kg (p<0.05).

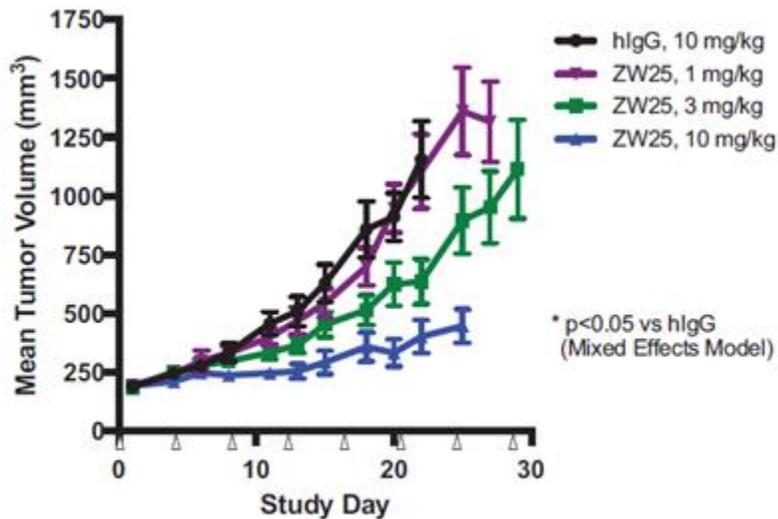
#### Exhibit 16: ZW25 Preclinical Efficacy In HER2 Low BrCa Derived Xenograft Model



Source: Zymeworks Inc.

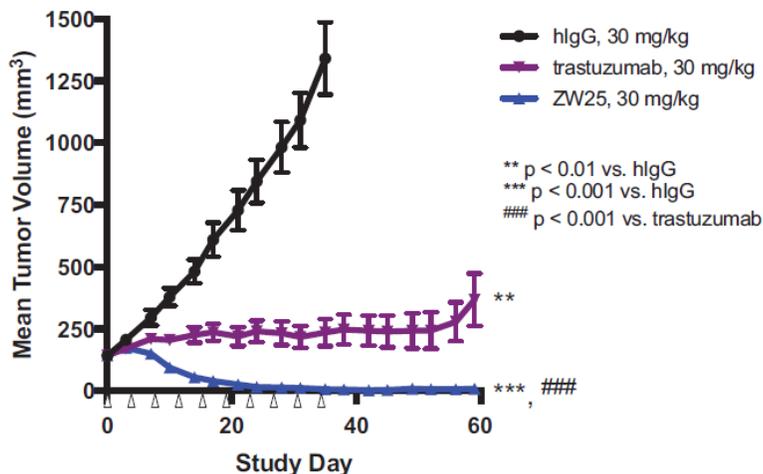
Similarly, ZYME has also demonstrated ZW25 efficacy in a HER2 high ovarian cancer derived xenograft model (see Exhibit 17). In this study, antibody therapy was administered twice weekly for four weeks in a blinded, randomized, placebo controlled format (n=10-12 mice/group). Treatment with ZW25 was shown to significantly inhibit the relative growth rates of tumor when compared to the hlgG control, and further that this effect appeared to be dose dependent (i.e. greater effect at higher dosage;  $p < 0.05$  in a mixed effects model). These results, while clearly early, suggest that ZW25 may show efficacy in HER2 high ovarian cancer, an indication for which HER2-targeted therapies are not currently approved.

**Exhibit 17: ZW25 Dose Dependent Efficacy In HER2 High Ovarian Cancer Patient Derived Xenograft Model**



Source: Zymeworks Inc.

Finally, ZYME has also demonstrated ZW25 superiority over Herceptin in a HER2 high gastric cancer patient derived xenograft model. In this study, antibody therapy was administered at 30 mg/kg twice weekly for five weeks in a blinded, randomized, placebo controlled fashion (n=10 mice/group). Treatment with ZW25 was associated with significant inhibition of the relative growth rate of tumors when compared to trastuzumab ( $p < 0.001$ ). Further, using modified RECIST criteria, ZW25 induced complete responses in 7/10 mice and partial responses in 3/10 mice in Day 35. All the responses induced by ZW25 were durable. At the completion of the study on day 59, 9/10 mice had complete responses and 1/10 had a partial response (see Exhibit 18). The results indicate that ZW25 may be an efficacious treatment for patients with HER2 high gastric cancers.

**Exhibit 18: ZW25 Efficacy In HER2 High Patient Derived Gastric Cancer Xenograft Model**

Response	ZW25 (n=10)	Trastuzumab (n=10)
Complete Response	7	0
Partial Response	3	1

Source: Zymeworks Inc.

From a preclinical safety perspective, ZW25 was shown to be well-tolerated by non-human primates in a repeat dose GLP toxicology study at up to 150 mg/kg administered every week for eight weeks followed by a five-week recovery period. Taken together, all of this data led to the filing of an IND for ZW25 in June 2016, and patient dosing commenced in September 2016 as part of an adaptive Phase I clinical trial.

### ZW25 Phase I Preliminary Data Shows Indications Of Durable Anti-Tumor Activity

ZW25 is currently being evaluated in a non-randomized, open-label, adaptive Phase I clinical trial (NCT02892123). The trial will evaluate ZW25 as a single agent (Part 1 and 2) and in combination (Part 3) in patients with locally advanced or metastatic solid tumors that express HER2. With respect to Part 3 of the trial, we anticipate that ZYME will likely explore potential combinations beyond standard of care chemotherapy, including options such as other small molecule targeted agents, other immuno-oncology agents, checkpoint inhibitors etc.

The primary objective of the ZW25 Phase I is to characterize the safety, tolerability, pharmacokinetic profile and maximum tolerated dose of ZW25. Secondary objectives include evaluation of preliminary anti-tumor activity, as well as identification of potential biomarkers of response.

On December 5, 2017, at the San Antonio Breast Cancer Symposium, ZYME provided its most recent update on Part 1 of the trial, the dose escalation portion, which is now complete. As per this update, a total of n=22 patients had been enrolled in the study, including patients with breast cancer (n=11), with gastric, gastroesophageal junction or esophageal cancer (n=8) and other HER2 expressing cancers (n=3). During this part of the trial, patients received ZW25 either weekly at three dose levels: 5 mg/kg (n=3), 10 mg/kg (n=6), 15 mg/kg (n=7), or alternatively, bi-weekly at 20 mg/kg (n=6) in cycles of four weeks each. All patients enrolled had received multiple prior regimens of systemic therapy for metastatic disease (range 1-10), and thus, represent a heavily pretreated population. We present an overview of the patient characteristics in Exhibit 19.

**Exhibit 19: ZW25 Patient Characteristics**

	Weekly			Bi-weekly	Total
	5 mg/kg (n=3)	10 mg/kg (n=6)	15 mg/kg (n=7)	20 mg/kg (n=6)	(n=22)
Median Age (range)	61 (58-64)	65 (31-73)	52 (36-70)	71 (27-75)	63 (27-75)
Male : Female	1 M : 2 F	4 M : 2 F	3 M : 4 F	1 M : 5 F	7 M : 15 F
ECOG Performance Status 0 : 1 (n)	0 : 3	2 : 4	2 : 5	0 : 6	4 : 18
HER2 Status <sup>1</sup> :					
High (IHC 3+ or IHC 2+/FISH+)	3	5	4	6	18
Low (HER2 IHC 1+/FISH-)	0	1	2	0	3
Heterogeneous	0	0	1	0	1
Median number systemic regimens for metastatic disease (range)	4 (4-7)	3 (2-8)	5 (1-7)	5 (3-10)	4 (1-10)
Tumor Type					
Breast	2	2	4	3	11
Gastric/GEJ/Esoophageal (GE)	1	3	2	2	8
Other <sup>2</sup>	0	1	1	1	3

Source: Beeram, et al. ESMO 2017

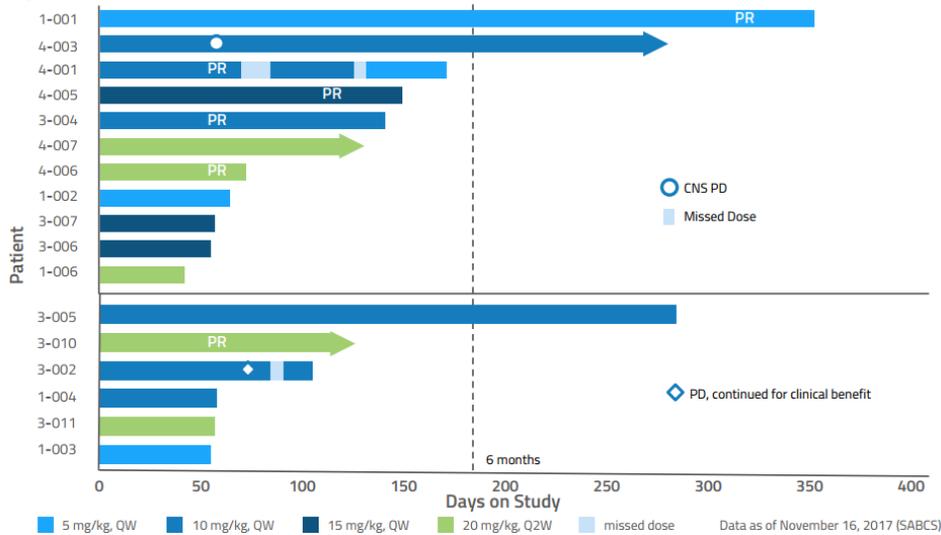
From a safety perspective, no dose-limiting toxicities were seen at any dose level or schedule. The most common adverse events were diarrhea (n=13), infusion reactions (n=11) and nausea (n=8). There were no treatment related serious adverse events, cardiac events or decreases in left ventricular ejection fraction, a well-known adverse effect of various chemotherapeutic agents.

While the primary objective of this Phase I trial was to determine safety and not efficacy, we are intrigued by the anti-tumor activity demonstrated by ZW25 therapy in what are essentially salvage line patients. We find this particularly interesting as almost all patients had progressed through treatment with both trastuzumab and pertuzumab, which bind the same epitopes as ZW25, thus seemingly confirming one of the key theoretical benefits of bispecific antibody therapeutic, namely delivering more therapeutic to targeted sites due to binding geometry.

Looking specifically at the trial results, the majority of patients with measurable disease had a decrease in target lesions per RECIST 1.1 criteria (n=10/14, 71%). The best overall response in 17 response-evaluable breast and GE patients was six partial responses (PR), three stable disease (SD) and eight progressive disease (PD) for an overall disease control rate of 53%.

In evaluating all of the data from the dose escalation study in aggregate but segregating into the breast cancer cohort and gastric/GEJ cohort, we find the results fairly compelling. Of the 11 breast cancer patients, all were HER2-high and had received a median of six prior HER2 targeted regimens for metastatic breast cancer including trastuzumab (n=11), T-DM1 (n=11), pertuzumab (n=9), lapatinib (n=7) as well as other investigational agents. The median time on drug as of this update was 119 days (range 41 – 348) and the best overall response (BOR) in these salvage line patients was 5 PR (45%), 2 SD (18%) and 4 PD (36%), for an overall disease control rate of 64%. Notably, at least one PR was observed in each dose cohort (1 at 5 mg/kg, 2 at 10 mg/kg, 1 at 15 mg/kg and 1 at 20 mg/kg). In our view this increases our conviction that ZW25 is inducing a real anti-tumor effect as a single agent therapy. We believe the probability that this could be spontaneous regression, in each of these patients, across multiple dosing groups, is low.

Of the 6 gastric/GEJ patients evaluable for response, all had received a median of four prior systemic regimens, including trastuzumab. 3/5 patients with measurable disease had a decrease in tumor size with the 1 PR and 1 SD. Interestingly, the 1 PR seems to be highly encouraging with a 71% decrease in SLD from baseline at the end of the 4<sup>th</sup> cycle. Furthermore, the patient remains on drug after 115 days. We present a review of the breast cancer and gastric/GEJ patients in Exhibit 20.

**Exhibit 20: ZW25 In HER2-High Breast And Gastric/GEJ Cancer Patients**

Source: Zymeworks Inc.

Taken together, we believe the results generated in the dose escalation portion of the trial are quite compelling and certainly supports ZW25's further development as both a single agent and in combination with other anti-cancer therapeutics. We do, however, believe there is one aspect of the data worth addressing and that would be duration. Notably, while there were 3 patients that have remained on drug past 6 months, the average time on drug in the dose escalation cohort was approximately 125 days (with 3 patients still active). While we believe duration is an acceptable criticism of the data to date we would emphasize that the dose escalation phase had less than rigorous exclusion criteria which in our view significantly impacted ZYME's ability to generate robust duration data. For example, patients with known visceral disease or stable treated brain metastases were included in the trial. As a result of this somewhat relaxed inclusion/exclusion criteria we do not believe it is a coincidence that all three PD's in the breast cancer cohort were flagged PD due to CNS metastases meanwhile all had systemic (non-CNS) disease control (SD or PR) at the time of progression. It is worth consideration that perhaps with more rigorous inclusion/exclusion criteria, these patients would have remained on treatment for a significantly longer duration. We look forward to data from the dose expansion part of the trial which we believe has a high probability of putting our concerns around duration to rest.

**ZW25 Dose Expansion Is Currently Enrolling Patients**

Part 2 of the trial, the dose expansion portion, is currently enrolling patients. In this part of the trial, patients will be enrolled into one of four cohorts:

Cohort 1: HER2-high BrCa (n=15)

Cohort 2: HER2-high gastric cancer (n=15)

Cohort 3: HER2-intermediate BrCa (n=15)

Cohort 4: Other HER2-gene amplified cancers (i.e. a basket cohort, n=10)

Patients in Part 2 of the study will receive ZW25 20 mg/kg Q2W. These patients will be followed to further evaluate the safety of ZW25 as well as to explore anti-tumor activity. ZYME currently has recruitment sites up and running in the US as well as in Canada and ZYME has committed to providing an update on the dose expansion data at ASCO 2018 which we believe could represent a significant value inflection point for the company, particularly if it is able to demonstrate an overall disease control rate generally in line with what we have seen in the dose escalation data. To put this into context, management believes an overall disease control rate of 50% with 4 months durability data might be sufficient to enable them to receive breakthrough therapy

designation for ZW25 in HER2-High metastatic breast cancer. In our view, we believe management may be conservative in their estimation and a lower overall disease control rate in salvage line breast cancer patients may be sufficient. Either way, such results would see us revisiting our probability discount around ZW25 in our SOTP model which would have a material positive impact to our per share target.

## ZW25: Financial Analysis & Outlook

### We Believe ZW25 Has The Potential To Surpass \$600 mln In Annual Sales At Peak Penetration

It is estimated that in the US and EU5 (France, Germany, Italy, Spain and the UK), the annual incidence of HER2 expressing breast and gastroesophageal cancer is approximately 405,803 and 49,058, respectively, in each jurisdiction. Notably, approximately 81% of HER2-expressing breast cancers and 57% of patients with HER2-expressing gastric and gastroesophageal junction cancer have tumors that express low to intermediate levels of HER2, making them ineligible for treatment with currently approved HER2-targeted therapies, such as Herceptin and Perjeta (therapeutics which delivered \$7.2 bln and \$2.3 bln in 2017 sales, respectively). There is clearly a need for HER2 targeted therapeutics that can effectively treat patients which Herceptin and Perjeta fail to address.

Zymeworks considers first-line, Stage III inoperable and Stage IV breast cancer, HER2 2+, non-FISH amplified as their lead indication for ZW25. The company estimates that the annual incidence of this patient group will reach 30,400 in the US and EU5, in aggregate, by 2023. ZW25 may also be effective as either a neoadjuvant or adjuvant therapy for the treatment of HER2 low and intermediate expressing, early stage breast cancer. Finally, there are a number of other cancers that express HER2 at varying levels that ZW25 may prove effective for, such as ovarian cancer.

In order to derive our sales estimates for ZW25, we take an extremely conservative approach by assuming ZW25 is only approved as a follow-on treatment for 2<sup>nd</sup>, 3<sup>rd</sup> or 4<sup>th</sup> line HER2 high metastatic breast cancers. In the US, we assume an annual BrCa incidence of 250,000, growing 1% Y/Y. We assume 20% of BrCa patients have high HER2 expression, and of those patients we assume 30% have metastatic disease (irrespective of de novo or relapse). In fact, we assume all metastatic BrCa patients receiving first line therapy have not received adjuvant therapy, and thus, assume 1<sup>st</sup> line response rates of 50%. We assume 80% of 2<sup>nd</sup> line patients to progress to 3<sup>rd</sup> line and 80% of 3<sup>rd</sup> line patients to 4<sup>th</sup> line treatment. We assume product launch in 2022, with penetration assumptions increasingly more aggressive in each respective line, but starting at 2% in 2<sup>nd</sup> line, 4% in 3<sup>rd</sup> line and 6% in 4<sup>th</sup> line. We assume peak penetration seven years post launch, plateauing at 20% in 2<sup>nd</sup> line, 20% in 3<sup>rd</sup> line and 40% in 4<sup>th</sup> line. We model sales through to 2035, when ZW25 comes off patent. We assume a net launch price of \$65,000 per patient year for ZW25, irrespective of treatment duration (in line with an average annual cycle of Herceptin and Perjeta).

For the EU5, we assume a slightly higher annual BrCa incidence of 275,000 and assume discounted pricing of \$45,000 per patient year. All other assumptions remain as above. Taken together, our assumptions result in peak annual sales (by 2028) for ZW25 of \$361 mln in the US (see Exhibit 21) and \$275 mln in the EU5 (see Exhibit 22).

We stress that we believe we are being extremely conservative with our estimates as ZW25 effectiveness could support 1<sup>st</sup> line use or could support use in neoadjuvant or adjuvant treatment of HER2 low and intermediate expressing early stage BrCa. This would present significant upside to our estimates. As would follow-on oncology indications such as gastric or ovarian HER2 expressing cancers as well as additional jurisdictions not modeled in this report. We note that building in a broader BrCa indication as well as follow-on HER2 positive cancer indications would result in peak sales estimates many multiples larger relative to what we are projecting.

**Exhibit 21: ZW25 US Sales Estimates**

<b>All Amounts in US\$</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
Annual US BrCa Incidence	250,000	252,500	255,025	257,575	260,151	262,753	265,380	268,034	270,714	273,421	276,156	278,917	281,706
% HER2 High	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
% HER2 High Metastatic	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Pts. Progressing to 2nd line	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Market Penetration (%)	2.0%	3.5%	5%	8%	12%	15%	20%	20%	20%	20%	20%	20%	20%
Ttl. # of Treated Patients	150	265	383	580	937	1,182	1,592	1,608	1,624	1,641	1,657	1,674	1,690
Net Cost per Treated Patient	\$65,000	\$66,365	\$67,759	\$69,182	\$70,634	\$72,118	\$73,632	\$75,178	\$76,757	\$78,369	\$80,015	\$81,695	\$83,411
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$9,750</b>	<b>\$17,595</b>	<b>\$25,920</b>	<b>\$40,094</b>	<b>\$66,152</b>	<b>\$85,271</b>	<b>\$117,243</b>	<b>\$120,902</b>	<b>\$124,676</b>	<b>\$128,567</b>	<b>\$132,579</b>	<b>\$136,717</b>	<b>\$140,984</b>
<b>All Amounts in US\$</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
2nd Line Patients	7,500	7,575	7,651	7,727	7,805	7,883	7,961	8,041	8,121	8,203	8,285	8,368	8,451
% Progressing to 3rd Line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	4.0%	6.0%	9%	12%	15%	18%	20%	20%	20%	20%	20%	20%	20%
Ttl. # of Treated Patients	240	364	551	742	937	1,135	1,274	1,287	1,299	1,312	1,326	1,339	1,352
Net Cost per Treated Patient	\$65,000	\$66,365	\$67,759	\$69,182	\$70,634	\$72,118	\$73,632	\$75,178	\$76,757	\$78,369	\$80,015	\$81,695	\$83,411
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$15,600</b>	<b>\$24,130</b>	<b>\$37,325</b>	<b>\$51,320</b>	<b>\$66,152</b>	<b>\$81,860</b>	<b>\$93,794</b>	<b>\$96,722</b>	<b>\$99,740</b>	<b>\$102,853</b>	<b>\$106,063</b>	<b>\$109,374</b>	<b>\$112,787</b>
<b>All Amounts in US\$</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
3rd Line Patients	6,000	6,060	6,121	6,182	6,244	6,306	6,369	6,433	6,497	6,562	6,628	6,694	6,761
% Progressing to 4th Line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	6.0%	9.0%	14%	18%	25%	32%	40%	40%	40%	40%	40%	40%	40%
Ttl. # of Treated Patients	288	436	686	890	1,249	1,614	2,038	2,058	2,079	2,100	2,121	2,142	2,164
Net Cost per Treated Patient	\$65,000	\$66,365	\$67,759	\$69,182	\$70,634	\$72,118	\$73,632	\$75,178	\$76,757	\$78,369	\$80,015	\$81,695	\$83,411
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$18,720</b>	<b>\$28,956</b>	<b>\$46,449</b>	<b>\$61,584</b>	<b>\$88,203</b>	<b>\$116,423</b>	<b>\$150,071</b>	<b>\$154,755</b>	<b>\$159,585</b>	<b>\$164,565</b>	<b>\$169,702</b>	<b>\$174,998</b>	<b>\$180,460</b>
<b>Total Revenue to ZYME (000s)</b>	<b>\$44,070</b>	<b>\$70,682</b>	<b>\$109,694</b>	<b>\$152,998</b>	<b>\$220,507</b>	<b>\$283,555</b>	<b>\$361,109</b>	<b>\$372,379</b>	<b>\$384,001</b>	<b>\$395,986</b>	<b>\$408,344</b>	<b>\$421,089</b>	<b>\$434,231</b>

Source: Raymond James Ltd.

**Exhibit 22: ZW25 EU5 Sales Estimates**

<b>All Amounts in US\$</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
Annual EU5 BrCa Incidence	275,000	277,750	280,528	283,333	286,166	289,028	291,918	294,837	297,786	300,763	303,771	306,809	309,877
% HER2 High	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
% HER2 High Metastatic	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Pts. Progressing to 2nd line	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Market Penetration (%)	2.0%	3.5%	5%	8%	12%	15%	20%	20%	20%	20%	20%	20%	20%
Ttl. # of Treated Patients	165	292	421	637	1,030	1,301	1,752	1,769	1,787	1,805	1,823	1,841	1,859
Net Cost per Treated Patient	\$45,000	\$45,945	\$46,910	\$47,895	\$48,901	\$49,928	\$50,976	\$52,047	\$53,140	\$54,256	\$55,395	\$56,558	\$57,746
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$7,425</b>	<b>\$13,399</b>	<b>\$19,739</b>	<b>\$30,533</b>	<b>\$50,377</b>	<b>\$64,937</b>	<b>\$89,285</b>	<b>\$92,072</b>	<b>\$94,945</b>	<b>\$97,909</b>	<b>\$100,964</b>	<b>\$104,115</b>	<b>\$107,365</b>
<b>All Amounts in US\$</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
2nd Line Patients	8,250	8,333	8,416	8,500	8,585	8,671	8,758	8,845	8,934	9,023	9,113	9,204	9,296
% Progressing to 3rd Line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	4.0%	6.0%	9%	12%	15%	18%	20%	20%	20%	20%	20%	20%	20%
Ttl. # of Treated Patients	264	400	606	816	1,030	1,249	1,401	1,415	1,429	1,444	1,458	1,473	1,487
Net Cost per Treated Patient	\$45,000	\$45,945	\$46,910	\$47,895	\$48,901	\$49,928	\$50,976	\$52,047	\$53,140	\$54,256	\$55,395	\$56,558	\$57,746
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$11,880</b>	<b>\$18,376</b>	<b>\$28,425</b>	<b>\$39,082</b>	<b>\$50,377</b>	<b>\$62,340</b>	<b>\$71,428</b>	<b>\$73,657</b>	<b>\$75,956</b>	<b>\$78,327</b>	<b>\$80,771</b>	<b>\$83,292</b>	<b>\$85,892</b>
<b>All Amounts in US\$</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
3rd Line Patients	6,600	6,666	6,733	6,800	6,868	6,937	7,006	7,076	7,147	7,218	7,291	7,363	7,437
% Progressing to 4th Line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	6.0%	9.0%	14%	18%	25%	32%	40%	40%	40%	40%	40%	40%	40%
Ttl. # of Treated Patients	317	480	754	979	1,374	1,776	2,242	2,264	2,287	2,310	2,333	2,356	2,380
Net Cost per Treated Patient	\$45,000	\$45,945	\$46,910	\$47,895	\$48,901	\$49,928	\$50,976	\$52,047	\$53,140	\$54,256	\$55,395	\$56,558	\$57,746
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$14,256</b>	<b>\$22,051</b>	<b>\$35,373</b>	<b>\$46,899</b>	<b>\$67,170</b>	<b>\$88,661</b>	<b>\$114,285</b>	<b>\$117,852</b>	<b>\$121,530</b>	<b>\$125,323</b>	<b>\$129,234</b>	<b>\$133,268</b>	<b>\$137,427</b>
<b>Total Revenue to ZYME (000s)</b>	<b>\$33,561</b>	<b>\$53,827</b>	<b>\$83,537</b>	<b>\$116,514</b>	<b>\$167,925</b>	<b>\$215,938</b>	<b>\$274,998</b>	<b>\$283,581</b>	<b>\$292,431</b>	<b>\$301,558</b>	<b>\$310,970</b>	<b>\$320,675</b>	<b>\$330,684</b>

Source: Raymond James Ltd.

## ZW49: ZYME's Near Term Second Clinical Asset

### ZW49: A Biparatopic Anti-HER2 Antibody Drug Conjugate

On March 14, 2018, ZYME announced that it would be pushing ahead, into clinical development, a novel ADC candidate developed utilizing the ZymeLink platform, which was acquired as part of the company's 2016 acquisition of Kairos Therapeutics (discussed above). Specifically, ZYME announced that this asset, named ZW49, would advance into the clinic in lieu of its predicate ADC candidate ZW33, based on ZW49's superior therapeutic window. ZW49 is a biparatopic anti-HER2 ADC that is based on the same antibody framework as ZW25 and takes advantage of ZW25's high levels of antibody-targeted internalization to deliver a proprietary ZymeLink cytotoxic payload, N-acyl sulfonamide auristatin, conjugated via a protease cleavable linker.

Prior to discussing the data supporting ZYME's strategic decision to advance ZW49, we believe it is prudent to review the data surrounding the predicate asset, ZW33, in order to understand that while ZW33 generated extremely compelling preclinical results, superior data generated from ZW49 suggested eventual self-cannibalization of ZYME's anti-HER2 ADC's. Ultimately, in our view, ZYME's decision was a prudent one from a capital allocation and resource conservation perspective.

### ZW33: The Predicate Biparatopic Anti-HER2 Antibody Drug Conjugate

Similar to ZW49, ZW33 is a biparatopic anti-HER2 ADC that is based on the same antibody framework as ZW25 (i.e., binds the same epitopes as trastuzumab and pertuzumab). However, unlike ZW25, ZW33 is armed with a cytotoxic payload, the potent cytotoxin emtansine, or DM1. DM1 is a well-characterized and clinically validated antibody drug conjugate cytotoxin that destabilizes tubulin and selectively inhibits cell division in rapidly dividing tissues.

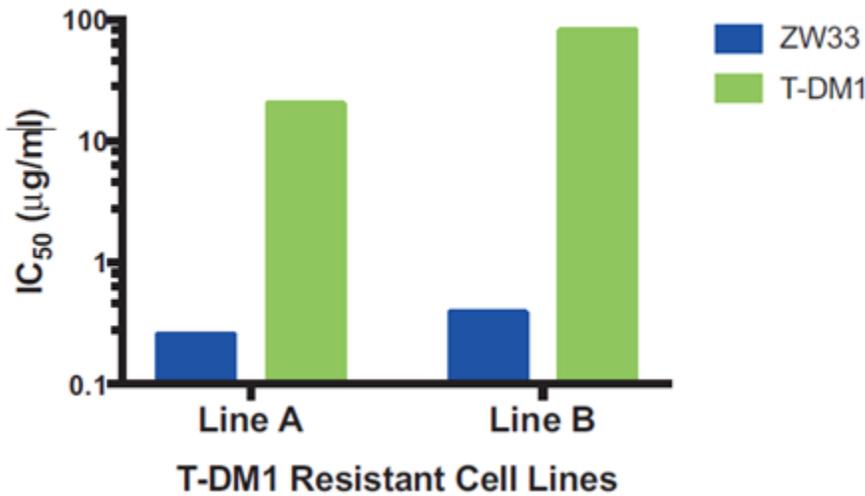
The approved breast cancer ADC, Kadcyra, also utilizes DM1 as its cytotoxic payload. Compared to Kadcyra, ZW33 preclinical data indicated a greater therapeutic effect due to its more effective ability to bind HER2 on tumor cells, which in turn should lead to enhanced HER2 mediated internalization and toxin mediated cytotoxicity. Additionally, ZW33 much alike what we will see with ZW49, had been expected to induce enhanced apoptosis, enhanced blockade of ligand-dependent and ligand-independent tumor growth, enhanced effector function mediated cytotoxicity and enhanced phagocytosis and presentation of tumor antigen.

### ZW33 Preclinical Data Suggests Efficacy In Resistant And Refractory Models Of HER2 Expressing Cancers

ZYME conducted preclinical studies which demonstrated that ZW33 can inhibit tumor growth, including complete regressions, in multiple trastuzumab-resistant xenograft models. Furthermore, breast cancer cell lines with acquired resistance to trastuzumab or to T-DM1 (Kadcyra) remained sensitive to growth inhibition by ZW33. ZW33 was also shown to be more efficacious than T-DM1 in trastuzumab-resistant patient derived breast cancer models. Finally, ZW33 has been demonstrated to induce regression of aggressive tumors as a 2<sup>nd</sup> line therapy in ovarian and breast cancer xenograft models. Together, these data suggest efficacy in resistant and refractory models of HER2 expressing cancer.

In the first study we will review, breast cancer cell lines with defined HER2 status were developed *in vivo* to have acquired resistance to T-DM1. Cells were then treated with serial dilutions of either ZW33 or T-DM1. The concentration required to inhibit 50% of cell culture growth (IC<sub>50</sub>) was significantly lower for ZW33 compared to T-DM1 (see Exhibit 23).

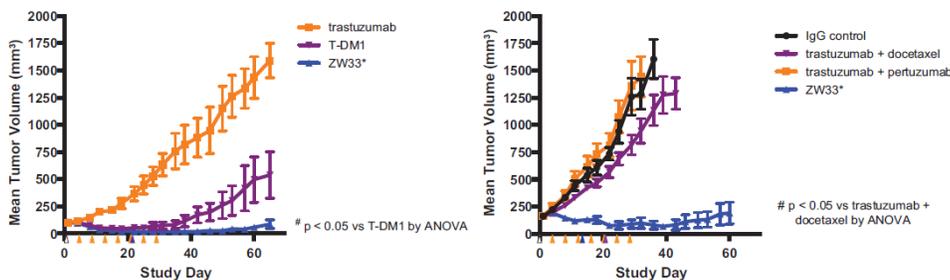
**Exhibit 23: ZW33 Retains Potency Against T-DM1 Resistant Cell Lines**



Source: Zymeworks Inc.

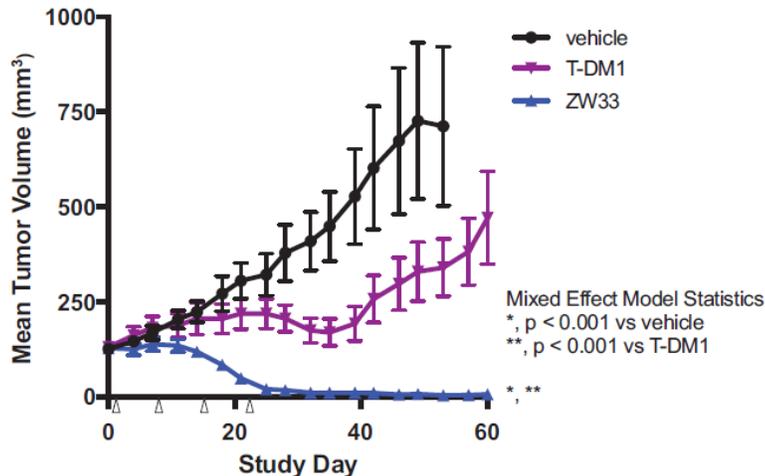
In the next noteworthy preclinical study, a first-generation ZW33 demonstrated superior tumor growth inhibition relative to other HER2 targeted therapies in a trastuzumab-resistant HER2 high xenograft tumor model. In the left panel of Exhibit 24, trastuzumab was administered at 15 mg/kg to load, and then at 10 mg/kg twice weekly for four weeks. T-DM1 and ZW33 were administered at 10 mg/kg to lead and then at 5 mg/kg on Day 22. In the study illustrated in the right panel of Exhibit 24, ZW33 was administered at 10 mg/kg on Days 1 and 14 (n=7 mice/group), trastuzumab + pertuzumab at 5 mg/kg each twice weekly for four weeks and docetaxel was administered at 20 mg/kg on Day 1 and Day 22 intraperitoneally (n=8-10 mice/group). In both cases, ZW33 significantly inhibited tumor growth compared to other HER2 targeted therapies (p<0.05).

**Exhibit 24: ZW33 Is Superior To Other HER2 Targeted Therapies In BrCa Xenograft Model**



Source: Zymeworks Inc.

In the final study worth discussion, ZYME demonstrated that ZW33 was able to achieve complete responses in a patient derived tumor model of serous adenocarcinoma of the ovary. In this blinded, randomized, placebo controlled study (n=10 mice/group), ZW33 or T-DM1 was administered at 5 mg/kg weekly for 4 weeks. Treatment with ZW33 significantly inhibited the relative growth rate of tumors compared to T-DM1 (p<0.001). Using modified 3D RECIST criteria on Day 53, ZW33 induced complete responses in 8/10 mice and partial responses in 2/10 mice.

**Exhibit 25: ZW33 Efficacy In HER2 Expressing Patient Derived Ovarian Cancer Xenograft**

Efficacy Criteria	ZW33 (n=10)	T-DM1 (n=10)
Tumor Growth Inhibition (%)	313%	65%
<b>3D RECIST Scores</b>		
Complete Response	8	0
Partial Response	2	1
Stable Disease	-	3
Progressive Disease	-	6

Source: Zymeworks Inc.

From a safety perspective, ZW33 was evaluated in a repeat-dose GLP toxicology pharmacokinetics study in non-human primates administered weekly for eight weeks followed by an eight-week recovery period. Based on preliminary results, ZYME had previously suggested the no observed adverse effect level of ZW33 is 3 mg/kg. Previously, ZYME had anticipated launching a Phase I clinical trial for ZW33 in late 2017 or early 2018. However, as we discussed above, the company made the strategic decision to advance an alternate ADC candidate, ZW49, in light of its superior therapeutic window attributable to its use of ZYME's proprietary ZymeLink ADC platform.

### ZW49 Is Superior To ZW33

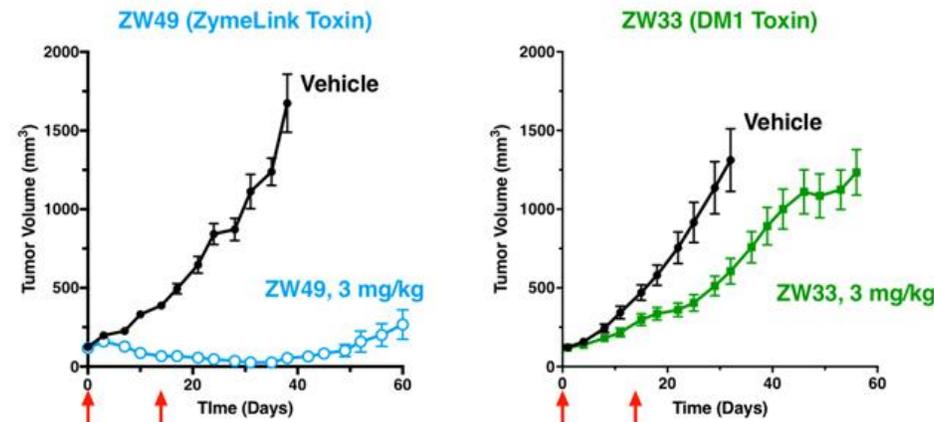
As mentioned above, while ZW33 generated highly compelling preclinical results, ZYME has recently unveiled data suggesting that a subsequent biparatopic anti-HER2 ADC candidate, ZW49, which utilizes a proprietary ZymeLink cytotoxic payload, N-acyl sulfonamide auristatin as opposed to emtansine, conjugated via a protease cleavable linker is superior to ZW33.

In short, ZYME recently submitted two abstracts to AACR, the results from which will be presented in further detail at the conference on April 17<sup>th</sup>, 2018. In the first abstract ZYME demonstrates that three monoclonal antibodies against three known clinical targets, when conjugated to N-acyl sulfonamide auristatin, had similar binding affinities and cytotoxicity in vitro when compared to the same antibodies conjugated to MMAE or DM4. In a NHP tolerability/PK study, all N-acyl sulfonamide auristatin conjugates were tolerated at doses up to 18 mg/kg compared to the controls which showed severe to life-threatening neutropenia at lower doses.

In the second abstract, ZYME demonstrates that N-acyl sulfonamide auristatin payload conjugation to ZW25 does not affect the antibody's binding to HER2 expressing cells. Furthermore, ZYME discusses potent in vitro and in vivo cytotoxicity with ZW49 administration.

For example, in mice bearing HER2 high tumors, two doses of ZW49 at 3 mg/kg (n=7) administered two weeks apart generated tumor regressions (Exhibit 26, left panel). To put this effect into perspective, on the right panel of Exhibit 26, the same xenograft model received two doses of ZW33 at 3 mg/kg (n=15), administered two weeks apart. The results clearly demonstrate ZW49's superiority in this specific model.

#### Exhibit 26: ZW49 Induces Superior Tumor Regression in a HER2 High PDX Model



Source: Zymeworks Inc.

Additionally, while the data has not yet been revealed specifically, ZYME has suggested that treatment with ZW49 resulted in anti-tumor activity in patient-derived xenograft models with lower levels of HER2 expression that do not respond to approved HER2-targeted therapies including T-DM1, or to ZW33.

Finally, ZYME has also disclosed that ZW49 was evaluated in a single-dose pharmacokinetic and tolerability study and repeat-dose toxicology study in NHP's. In the toxicology study, ZW49 was administered at 9 or 12 mg/kg every two weeks for five weeks. The no observed adverse effect level (NOAEL) was determined to be 12 mg/kg. In comparison, the NOAEL for ZW33 was determined to be 3 mg/kg when administered weekly for 38 weeks.

The data above suggest improved anti-tumor activity and tolerability of ZW49 vs. ZW33, and thus it is being advanced in lieu of ZW33.

#### ZW49 IND Expected To Be Filed In 2018

ZYME plans to evaluate ZW49 as a monotherapy in a non-randomized, open-label, Phase I trial for which the company anticipates filing its IND in 2018. We believe it is likely that first patient dosed could occur in 1H19. The primary objective of the trial will be to characterize the safety, tolerability, pharmacokinetics, and maximum tolerated dose of ZW49. Secondary objectives will include evaluation of the preliminary anti-tumor activity of ZW33, as well as an exploration of potential biomarkers of response. Depending on the data generated in the trial, subsequent development of ZW33 may expand to include early lines of therapy in HER2 high breast and HER2 high gastric cancer as well as early lines of therapy in patients whose tumors express lower levels of HER2 and are thus ineligible for treatment with HER-2 targeted therapies.

Eventually, in our view, ZYME would benefit by conducting head-to-head clinical trials against Kadcykla. Should ZW49 demonstrate superiority as the preclinical data suggests, ZW49 could in time replace Kadcykla as the preferred therapy for second line treatment of HER2+ metastatic cancer. Ultimately, ZW49 could be used as a follow-on therapy for ZW25, mirroring the development strategy employed for Kadcykla as a follow-on therapy for Herceptin.

## ZW49: Financial Analysis & Outlook

### We Believe ZW49 Is Likely To Be Utilized In Later Lines Of Therapy

In order to derive our sales estimates for ZW49, we assume that the therapy is only utilized in 3<sup>rd</sup> and 4<sup>th</sup> line HER2 high expressing metastatic breast cancer. Our assumptions for patients progressing to 3<sup>rd</sup> and 4<sup>th</sup> line are as we detailed in our ZW25 sales assumptions. Material differences in our ZW49 assumptions largely revolve around net pricing, moderately more conservative penetration estimates and launch year timing. We assume ZW49 will launch in 2025 and assume a net cost of \$100,000 per patient year in the US and \$70,000 per patient year in the EU5. Our assumptions result in peak annual sales (by 2031) for ZW49 of \$253 mln in the US (see Exhibit 26) and \$194 mln in the EU5 (see Exhibit 27).

Once again, we note that our estimates are overly conservative as ZW49 effectiveness could support earlier use. Follow-on oncology indication and additional jurisdictions also present material upside to our estimates which if realized could result in sales that are multiples higher than what we are projecting in our model.

**Exhibit 27: ZW49 US Sales Estimates**

<b>All Amounts in US\$</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
Annual US BrCa Incidence	250,000	252,500	255,025	257,575	260,151	262,753	265,380	268,034	270,714	273,421
% HER2 High	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
% HER2 High Metastatic	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
% Progressing to 2nd line	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
% Progressing to 3rd line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	2.0%	3.0%	5%	8%	11%	13%	15%	15%	15%	15%
Ttl. # of Treated Patients	120	182	306	495	687	820	955	965	975	984
Net Cost per Treated Patient	\$100,000	\$102,100	\$104,244	\$106,433	\$108,668	\$110,950	\$113,280	\$115,659	\$118,088	\$120,568
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$12,000</b>	<b>\$18,562</b>	<b>\$31,902</b>	<b>\$52,636</b>	<b>\$74,633</b>	<b>\$90,956</b>	<b>\$108,224</b>	<b>\$111,602</b>	<b>\$115,085</b>	<b>\$118,677</b>
<b>All Amounts in US\$</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
3rd Line Patients	6,000	6,060	6,121	6,182	6,244	6,306	6,369	6,433	6,497	6,562
% Progressing to 4th Line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	3.0%	5.0%	7%	10%	14%	20%	25%	25%	25%	25%
Ttl. # of Treated Patients	144	242	343	495	699	1,009	1,274	1,287	1,299	1,312
Net Cost per Treated Patient	\$100,000	\$102,100	\$104,244	\$106,433	\$108,668	\$110,950	\$113,280	\$115,659	\$118,088	\$120,568
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$14,400</b>	<b>\$24,749</b>	<b>\$35,730</b>	<b>\$52,636</b>	<b>\$75,990</b>	<b>\$111,946</b>	<b>\$144,299</b>	<b>\$148,803</b>	<b>\$153,447</b>	<b>\$158,236</b>
<b>Total Revenue to ZYME (000s)</b>	<b>\$26,400</b>	<b>\$43,311</b>	<b>\$67,632</b>	<b>\$105,272</b>	<b>\$150,623</b>	<b>\$202,901</b>	<b>\$252,524</b>	<b>\$260,405</b>	<b>\$268,532</b>	<b>\$276,913</b>

Source: Raymond James Ltd.

**Exhibit 28: ZW49 EU5 Sales Estimates**

<b>All Amounts in US\$</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
Annual US BrCa Incidence	275,000	277,750	280,528	283,333	286,166	289,028	291,918	294,837	297,786	300,763
% HER2 High	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
% HER2 High Metastatic	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
% Progressing to 2nd line	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
% Progressing to 3rd line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	2.0%	3.0%	5%	8%	11%	13%	15%	15%	15%	15%
Ttl. # of Treated Patients	132	200	337	544	755	902	1,051	1,061	1,072	1,083
Net Cost per Treated Patient	\$70,000	\$71,470	\$72,971	\$74,503	\$76,068	\$77,665	\$79,296	\$80,961	\$82,662	\$84,398
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$9,240</b>	<b>\$14,293</b>	<b>\$24,564</b>	<b>\$40,530</b>	<b>\$57,468</b>	<b>\$70,036</b>	<b>\$83,333</b>	<b>\$85,934</b>	<b>\$88,616</b>	<b>\$91,381</b>
<b>All Amounts in US\$</b>	<b>2025</b>	<b>2026</b>	<b>2027</b>	<b>2028</b>	<b>2029</b>	<b>2030</b>	<b>2031</b>	<b>2032</b>	<b>2033</b>	<b>2034</b>
3rd Line Patients	6,600	6,666	6,733	6,800	6,868	6,937	7,006	7,076	7,147	7,218
% Progressing to 4th Line	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Market Penetration (%)	3.0%	5.0%	7%	10%	14%	20%	25%	25%	25%	25%
Ttl. # of Treated Patients	158	267	377	544	769	1,110	1,401	1,415	1,429	1,444
Net Cost per Treated Patient	\$70,000	\$71,470	\$72,971	\$74,503	\$76,068	\$77,665	\$79,296	\$80,961	\$82,662	\$84,398
Price Appreciation	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
<b>Net Sales (\$000s)</b>	<b>\$11,088</b>	<b>\$19,057</b>	<b>\$27,512</b>	<b>\$40,530</b>	<b>\$58,512</b>	<b>\$86,198</b>	<b>\$111,110</b>	<b>\$114,578</b>	<b>\$118,154</b>	<b>\$121,842</b>
<b>Total Revenue to ZYME (000s)</b>	<b>\$20,328</b>	<b>\$33,349</b>	<b>\$52,077</b>	<b>\$81,059</b>	<b>\$115,980</b>	<b>\$156,234</b>	<b>\$194,443</b>	<b>\$200,512</b>	<b>\$206,770</b>	<b>\$213,223</b>

Source: Raymond James Ltd.

## Strategic Partnerships and Collaborations

### \$5.5 bln In “Biobucks” Committed Through Strategic Partnerships To Date

The inherent value in Zymeworks’ proprietary platforms to optimize the efficacy and safety of protein therapeutics is highly sought after by Big Pharma. To date, ZYME has inked deals with six major biopharmaceutical companies: Celgene, GlaxoSmithKline, Eli Lilly, Merck, Daiichi Sankyo and JNJ. These partnerships in aggregate have the potential to provide ZYME with up to \$5.5 bln in non-dilutive development, regulatory and sales milestone payments. To date, ZYME has received over \$75 mln in the form of non-refundable upfront payments and milestones and is eligible to receive up to \$1.5 bln in development and \$4.0 bln in commercial milestone payments under its existing collaboration agreements. In many cases, ZYME is also eligible to receive tiered royalties on future product sales. Exhibit 29 illustrates ZYME’s existing partnerships and we present a brief review below.

#### Exhibit 29: Overview of ZYME’s Strategic Partnerships

Partners	Events	Programs	Enabling Platform(s)	Equity	Royalty % Range	Total Deal Size
	Announced: 2011 Milestone #1: 2012 Milestone #2: 2013 Expanded: 2014	Multiple Up to 3	Azymetric™ EFFECT™	-	Low-Mid Single Digit	190.75
	Announced: 2014 Expanded: 2014 Milestone #1: 2015 Milestone #2: 2016	Multiple Up to 5 (Includes Immuno-Oncology)	Azymetric™	C\$27M (Initial)	Low-Mid Single Digit	478.0
	Announced: 2015	Multiple Up to 8	Azymetric™	C\$10M (Initial)	Low-Mid Single Digit	1.32B
	Announced: 2015	Multiple Up to 10	EFFECT™	-	Low Single Digit	1.10B
	Announced: 2016	Multiple Up to 6	Azymetric™	-	Low-Mid Single Digit	908.0
	Announced: 2016 Milestone #1: 2017	One (Immuno-Oncology)	Azymetric™ EFFECT™	-	Low Single Digit-10	149.9
	Announced: 2017	Multiple Up to 6 Option for 2 Additional	Azymetric™ EFFECT™	-	Low-Mid Single Digit	1.45B
<b>Total: US \$5.5 Billion</b>						

Source: Zymeworks Inc.

#### Merck: \$186 mln In Milestones Remaining

ZYME entered into a research and license agreement with Merck in August 2011, which was subsequently amended and restated in December 2014, to develop and commercialize three antibodies utilizing the Azymetric and EFFECT platforms. ZYME has received \$1.25 mln upfront (2011) and research milestones totaling \$3.5 mln (\$2.0 mln in 2012 and \$1.5 mln in 2013). Remaining potential payments include: \$6.0 mln for completion of IND-enabling studies, \$66.0 mln in development milestones and \$114.0 mln in commercial milestones. ZYME is also eligible to receive tiered royalties in the low to mid-single digits on product sales. Merck funds a portion of ZYME’s internal and external research costs in support of the collaboration. Finally, in September 2017, Merck provided formal notification to ZYME of its plans to advance a bispecific drug candidate into preclinical development.

***Eli Lilly: \$474 mln In Milestones Remaining***

ZYME entered into a research and license agreement with Lilly in December 2013, to develop and commercialize one bispecific antibody, with the option for a second, utilizing the Azymetric platform. A second agreement was entered into with Lilly in October 2014, to include three additional bispecific antibodies. ZYME has received \$1.0 mln upfront (2013) and research milestones totaling \$3.0 mln (\$1.0 mln in 2015 and \$2.0 mln in 2016). Remaining potential payments include: \$5.0 mln in additional research milestones, \$28.0 mln for completion of IND-enabling studies, \$76.0 mln in development milestones and \$365.0 mln in commercial milestones. ZYME is also eligible to receive tiered royalties in the low to mid-single digits on product sales. In conjunction with the October 2014 deal, Lilly purchased approximately \$24 mln of ZYME common shares.

***Celgene: \$1.3 bln In Milestones Remaining***

ZYME entered into a research and license agreement with Celgene in December 2014 to develop and commercialize up to eight bispecific antibodies, utilizing the Azymetric platform. ZYME received \$8.0 mln upfront (2014). Remaining potential payments include: \$60 mln in commercial license option payments, development milestone payments of up to \$812 mln and commercial milestone payments of up to \$440 mln. ZYME is also eligible to receive tiered royalties in the low to mid-single digits on product sales. Celgene also has the right, prior to first dosing of a patient in a Phase III trial for a product, to buy down the royalty to a flat low single-digit rate with a payment of \$10 mln per percentage point. In addition, ZYME and Celgene entered into an equity subscription agreement under which Celgene paid \$8.6 mln for ZYME common shares.

***GSK: \$2.0 bln In Aggregate Milestones Remaining***

ZYME entered into a research and license agreement with GSK in December 2015, to develop and commercialize up to 10 new Fc-engineered monoclonal and bispecific antibodies, utilizing the Azymetric and EFECT platforms. ZYME entered into a second agreement with GSK in April 2016, to develop up to six bispecific antibodies utilizing the Azymetric platform. This may include the incorporation of new engineered Fc regions generated under the 2015 agreement. ZYME has received \$6.0 mln upfront (2016). Remaining potential payments include: \$1.1 bln in additional research milestones, \$152.0 mln in development milestones and \$720.0 mln in commercial milestones. ZYME is also eligible to receive tiered royalties in the low to mid-single digits on product sales. GSK also has the right, prior to first dosing of a patient in a Phase III trial for a product, to buy down the royalty by 1% with a payment of \$10 mln.

***Daiichi Sankyo: \$147 mln In Milestones Remaining***

ZYME entered into a collaboration and cross-license agreement with Daiichi in September 2016, to develop and commercialize one bispecific antibody utilizing the Azymetric and EFECT platforms. ZYME to date has received \$2.0 mln upfront (2016) and \$1.0 mln in milestone payments (2Q17). Remaining potential payments include: \$66.9 mln in development and commercial option payments and \$80.0 mln in commercial milestones. ZYME is also eligible to receive tiered royalties in the low single digits up to 10% on product sales. ZYME also gained non-exclusive rights to develop and commercialize up to three products using Daiichi's proprietary immune oncology antibodies, with royalties to Daiichi in the low single digits on sales of such products.

***Johnson & Johnson: \$1.40 bln In Milestones Remaining***

ZYME entered into a collaboration and license agreement with Janssen in November 2017, to develop and commercialize up to six bispecific antibodies (with an option exercise fee to expand to eight) directed to Janseen therapeutic targets utilizing the Azymetric and EFECT platforms. ZYME to date has received \$50.0 mln upfront (3Q17) and is eligible to receive development milestone payments of up to \$282.0 mln and commercial milestone payments of up to \$1.12 bln. Furthermore, ZYME is eligible to receive tiered royalties in the mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either until the licensed product is no longer covered by a valid patent claim or 10 years after the first commercial sale. On a licensed product-by-licensed product basis, prior to the first dosing of a patient in a Phase 3 clinical trial, Janssen will have the right to buy down the product royalty by 1% with a payment of \$10 mln.

## Valuation & Recommendation

### SOTP Valuation Best Captures ZYME's Value

Zymeworks is a clinical stage biopharmaceutical company with one wholly owned asset currently in the clinic, one wholly owned asset which is expected to enter the clinic by 2018YE and multiple pharmaceutical collaborations which, in aggregate, have the potential to generate \$5.5 bln in non-dilutive capital for the company. As such, we believe the most appropriate valuation methodology to capture the inherent value of ZYME's multiple endeavors is through a probability adjusted net present value, sum of the parts, analysis. Notably, while ZYME has a robust preclinical and discovery pipeline, we only attribute value to those assets which are in (or soon to be in) the clinic. We present our methodology below.

### We Value ZW25 At \$8.45 Per Share

As illustrated above, we currently only account for ZW25 US and EU5 sales from its use in 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> line mBrCa therapy. We assume ZW25 gains FDA and EMA regulatory approval in 2021 and is launched in 2022. We model out sales up to 2034, the year ZW25 loses patent exclusivity, notwithstanding any patent extension options available to the company. We assume a 40% FCF margin on sales, and discount FCFs back utilizing a 10% discount rate to arrive at our aggregate ZW25 NPV. Further, we probability adjust our NPV value at 30% to account for the likelihood of ZW25 clinical success. Notably, our assumed 30% probability of success is a 50% discount to the conditional probability of a Phase I oncology asset progressing to Phase II, however is a premium to the 6% conditional probability to approval. We believe our bullish probability assumption is warranted due to: 1) the fact that ZW25 binds well validated epitopes (specifically the same as Herceptin and Perjeta) which elicits a well validated biological cascade in a well characterized indication, 2) the preliminary anti-tumor efficacy demonstrated to date by ZYME, and 3) the fact that we only model out a small fraction of the commercial potential of this asset. Our valuation results in a per share value of \$8.45.

#### Exhibit 30: Valuation of ZW25

US\$MM (except per share)	
Discount rate	10%
PV of ZW25 US FCF (\$000's)	\$453.52
PV of ZW25 EU5 FCF (\$000's)	\$345.37
Probability of Success	30%
Probability Discounted Aggregate FCF	\$239.67
ZYME FD S/O	28.35
<b>ZW25 Per Share Value</b>	<b>\$8.45</b>

Source: Raymond James Ltd.

### We Value ZW49 At \$1.17 Per Share

While we typically only value clinical assets, ZYME anticipates filing its IND for ZW49 in 2018. As such, we have included this asset in our valuation, albeit utilizing a significant probability adjustment. We assume ZW49 gains FDA and EMA regulatory approval in 2024 and is launched in 2025. We model out sales up to 2034, the year ZW49 loses patent exclusivity, notwithstanding any patent extension options available to the company. We assume a 40% FCF margin on sales, and discount FCFs back utilizing a 10% discount rate to arrive at our aggregate ZW49 NPV. Seeing as how ZW49 is technically still a preclinical asset, we utilize a rather aggressive probability discount (particularly in light of the read-through ZW25 success would have on ZW49), which implies a 10% probability of success, which we will revisit as this asset progresses deeper into the clinic. Our valuation results in a per share value of \$1.17 for ZW49.

**Exhibit 31: Valuation of ZW49**

<b>US\$MM (except per share)</b>	
Discount rate	10%
PV of ZW49 US FCF (\$000's)	\$194.69
PV of ZW49 EU5 FCF (\$000's)	\$136.29
Probability of Success	10%
Probability Discounted Aggregate FCF	\$33.10
ZYME FD S/O	28.35
<b>ZW33 Per Share Value</b>	<b>\$1.17</b>

Source: Raymond James Ltd.

**Strategic Partnerships Contributes \$4.80 Per Share**

In order to determine the value of ZYME's strategic partnerships and research collaborations, we make the assumption that 10% of ZYME's aggregate potential milestone balance is paid out in commercial milestones. We attribute no value to research support revenue or future royalty streams. Specifically, we make the conservative assumption that the commercial milestones are met in 2028, which we then discount back at 15%. The resulting value is \$4.80 per share for ZYME's partnerships. Any additional partnerships or large development milestones would be viewed as upside to our valuation.

**Exhibit 32: Valuation of Strategic Partnerships and Collaborations**

<b>US\$MM (except per share)</b>	
Outstanding Payments	\$5,500.00
Portion Paid Out	10%
Payments Received	\$550.00
Discount Rate	15%
Discounted Periods	10
FD Shares Out (MMs)	28.3
<b>Per Share Value</b>	<b>\$4.80</b>

Source: Raymond James Ltd.

**Initiating With An Outperform, US\$18.00 Per Share Target**

We are initiating on Zymeworks with an Outperform recommendation and an US\$18.00 per share target (rounded up from \$17.51) based on our probability adjusted, net present value, sum-of-the-parts model. The remainder of our target valuation not detailed above is our per share cash allocation, utilizing ZYME's 2017 exit cash position of \$87.8 mln. While it is early days for Zymeworks, in our view, the company has generated highly compelling preclinical and clinical data utilizing its proprietary platform technologies. Furthermore, the company has entered into multiple high-profile, validating partnerships. Looking forward, we anticipate significant momentum in both expanding and novel partnership agreements, as well as substantial enhancements to ZYME's wholly owned therapeutic pipeline. As such, amongst Canada's early-stage biotechnology opportunities, we view ZYME as the Mother Of All Biotechnology (M.O.A.B) plays, for risk-tolerant investors.

**Exhibit 33: Summary of SOTP Valuation**

<b>SOTP Valuation Summary</b>	
ZW25	\$8.45
ZW49	\$1.17
Partnerships	\$4.80
Cash	\$3.10
<b>Per Share Target Price</b>	<b>\$17.51</b>

Source: Raymond James Ltd.

## Appendix A: Financial Statements

### Exhibit 34: Zymeworks Income Statement

Fiscal YE Dec. 31 (US\$000s, except where noted)	2015A	2016A	2017A				2017A	2018E	2019E	2020E
			1QA	2QA	3QA	4QA				
<b>Revenue</b>										
Research & dev. collabs.	9660	11009	230	1,342	119	50,071	\$51,762	\$-	\$-	\$-
<b>Operating Expenses</b>										
R&D	24,654	36,816	9,058	8,289	11,525	12,877	41,749	50,934	61,121	61,121
Gov't grants & credits	(251)	(1,265)	(218)	-	-	(857)	(1,075)	-	-	-
G&A	5,217	12,554	6,259	2,285	5,291	4,715	18,550	19,478	20,451	21,474
Impairment on IPR&D	-	768	1,536	-	-	-	1,536	1,613	1,693	1,778
<b>EBITDA</b>	(19,466)	(36,839)	(15,817)	(8,544)	(15,979)	33,990	\$(6,350)	\$(68,910)	\$(75,670)	\$(61,153)
Amortization of intang.	214	484	270	241	270	277	1,058	-	-	-
Depreciation of P&E	280	541	318	447	448	377	1,590	1,501	5,902	21,442
<b>EBIT</b>	(19,960)	(37,864)	(16,405)	(9,232)	(16,697)	33,336	(8,998)	(70,411)	(81,572)	(82,594)
Interest & other expense	(18)	(950)	(227)	(179)	(2)	(484)	(892)	-	-	-
Change in value of warrant liabs.	-	(808)	555	1,578	187	130	2,450	-	-	-
Accretion on LTD	-	(576)	(88)	(160)	-	-	(248)	-	-	-
Interest & other income	324	308	50	328	210	155	743	-	-	-
F/X (gain) / loss	518	927	189	(64)	107	(135)	97	-	-	-
Loss on debt extinguishment	-	-	-	(3,114)	-	-	(3,114)	-	-	-
Equity loss on invest.	-	(98)	-	-	-	-	-	-	-	-
Gain on value of equity invest.	-	177	-	-	-	-	-	-	-	-
<b>EBT</b>	\$(19,136)	\$(38,884)	\$(15,926)	\$(10,843)	\$(16,195)	\$33,002	(9,962)	(70,411)	(81,572)	(82,594)
Income tax expense	(18)	(430)	-	(162)	(35)	(232)	(429)	-	-	-
Def. income tax recovery	(16)	5,505	-	37	(15)	(37)	(15)	-	-	-
<b>Net Income / (Loss)</b>	\$(19,170)	\$(33,809)	\$(15,926)	\$(10,968)	\$(16,245)	\$32,733	\$(10,406)	\$(70,411)	\$(81,572)	\$(82,594)
Weighted Average S/O										
Basic	11,266	12,737	13,184	20,916	25,339	25,339	21,249	21,271	21,271	21,271
Fully Diluted	11,266	12,737	13,330	21,039	25,349	25,349	21,321	21,321	21,321	21,321
<b>Earnings Per Share</b>										
Basic	\$(1.70)	\$(2.65)	\$(1.21)	\$(0.52)	\$(0.64)	\$1.86	\$(0.51)	\$(3.31)	\$(3.83)	\$(3.88)
Fully Diluted	\$(1.70)	\$(2.65)	\$(1.25)	\$(0.52)	\$(0.64)	\$1.79	\$(0.62)	\$(3.30)	\$(3.83)	\$(3.87)

Source: Zymeworks Inc., Raymond James Ltd.

**Exhibit 35: Zymeworks Balance Sheet**

Fiscal YE Dec. 31 (US\$000s, except where noted)	2015A	2016A	2017A				2017A
			1QA	2QA	3QA	4QA	
<b>ASSETS</b>							
Current Assets							
Cash & Cash Equivalents	\$11,519	\$16,437	\$10,446	\$26,001	\$12,332	\$35,946	\$35,946
Short-term investments	3,641	23,824	16,343	36,482	36,761	51,851	51,851
SR&ED & IRAP receivables	759	1,660	1,888	1,719	1,788	2,092	2,092
Accounts receivables	1,506	2,647	468	1,429	180	238	238
Deferred Tax Asset	254	1,916	3,468	4,668	3,372	2,208	2,208
<b>Total current assets</b>	<b>17,679</b>	<b>46,484</b>	<b>32,613</b>	<b>70,299</b>	<b>54,433</b>	<b>92,335</b>	<b>92,335</b>
Non-Current Assets							
Def. financing fees	360	1,560	3,118	-	-	-	-
Acquired R&D	-	19,932	18,396	18,396	18,396	18,396	18,396
Goodwill	-	12,016	12,016	12,016	12,016	12,016	12,016
LT prepaid assets	4,185	1,483	1,006	1,280	1,248	1,215	1,215
Property & equipment	781	6,721	7,740	7,427	7,540	7,178	7,178
Intangible assets	144	699	432	219	1,000	748	748
Deferred tax assets	-	5,100	4,732	4,907	5,091	67	67
<b>Total Assets</b>	<b>\$23,149</b>	<b>\$93,995</b>	<b>\$80,053</b>	<b>\$114,544</b>	<b>\$99,724</b>	<b>\$131,955</b>	<b>\$131,955</b>
<b>LIAB. &amp; SHAREHOLDERS' EQUITY</b>							
Current Liabilities							
AP and accr. liabilities.	\$4,791	\$9,477	\$8,675	\$6,170	\$6,058	\$9,053	\$9,053
Warrant liabilities	-	4,342	3,787	1,665	1,478	1,348	1,348
Other curr. Liabs.	60	2,737	8,269	4,730	4,376	4,260	4,260
<b>Total Current Liabilities</b>	<b>4,851</b>	<b>16,556</b>	<b>20,731</b>	<b>12,565</b>	<b>11,912</b>	<b>14,661</b>	<b>14,661</b>
Non-current Liabilities							
Long-term Debt	-	4,417	4,518	-	-	-	-
Deferred tax liability	16	5,019	4,650	4,785	4,978	-	-
Other LT Liabilities	43	141	280	267	256	866	866
<b>Total Liabilities</b>	<b>4,910</b>	<b>26,133</b>	<b>30,179</b>	<b>17,617</b>	<b>17,146</b>	<b>15,527</b>	<b>15,527</b>
Redeemable pref. shares	-	58,860	58,860	-	-	-	-
Shareholders' Equity							
Common Stock	83,605	106,595	107,327	222,301	222,162	222,991	222,991
Additional Paid-in Cap.	5,215	6,856	4,062	6,489	8,524	8,812	8,812
Accumulated Other Comp. Inc.	(6,659)	(6,659)	(6,659)	(6,659)	(6,659)	(6,659)	(6,659)
Accumulated deficit	(63,922)	(97,790)	(113,716)	(125,204)	(141,449)	(108,716)	(108,716)
<b>Total Shareholders' Equity</b>	<b>18,239</b>	<b>9,002</b>	<b>(8,986)</b>	<b>96,927</b>	<b>82,578</b>	<b>116,428</b>	<b>116,428</b>
<b>Total Liabs., Prefs &amp; Share. Equity</b>	<b>\$23,149</b>	<b>\$93,995</b>	<b>\$80,053</b>	<b>\$114,544</b>	<b>\$99,724</b>	<b>\$131,955</b>	<b>\$131,955</b>

Source: Zymeworks Inc., Raymond James Ltd.

**Exhibit 36: Zymeworks Cash Flow Statement**

Fiscal YE Dec. 31 (\$000s, except where noted)	2017A		2017A				2017A
	2015A	2015A	1QA	2QA	3QA	4QA	
<b>Operating Activities</b>							
Net Loss	\$(19,170)	\$(33,809)	\$(15,926)	\$(10,968)	\$(16,245)	\$32,733	\$(10,406)
Non-Cash Adjustments:							
Depreciation of P&E	280	541	318	447	448	468	1,681
Amortization of Intang. Assets	214	484	270	241	270	277	1,058
Equity Loss on Invest.	-	98	-	-	-	-	-
Gain on Value of Invest.	-	(177)	-	-	-	-	-
Accretion on LT Debt	-	576	88	160	-	-	248
Loss on debt extinguishment	-	-	-	3,114	-	-	3,114
SBC	1,389	4,291	2,976	(1,614)	1,609	458	3,429
Def. Income Tax	16	(5,505)	-	(37)	15	37	15
Impairment on IPR&D	-	768	1,536	-	-	-	1,536
Change in Warrant Liab.	-	808	(555)	(1,578)	(187)	340	(1,980)
Unrealized FX (Gain) / loss	-	(954)	(154)	39	(66)	(73)	(254)
Changes in Op. Working Cap.							
Accounts Receivables	(1,363)	(592)	2,179	(961)	1,249	(58)	2,409
SR&ED & IRAP Rec.	1,660	(780)	(98)	170	(70)	(177)	(175)
Prepaid Exp. & Other Assets	(116)	(3,141)	(1,076)	(1,474)	1,328	1,195	(27)
Accounts Payable & Accr. Liabs.	2,417	1,934	(2,255)	(1,390)	(456)	3,743	(358)
Deferred Revenue	(7,515)	-	-	-	-	-	-
Income Taxes Payable	18	212	-	(96)	(47)	72	(71)
Cash Prov. By / (Used In) Op. Act.	\$(22,170)	\$(35,246)	\$(12,697)	\$(13,947)	\$(12,152)	\$39,015	\$219
<b>Financing Activities</b>							
Issuance of Pref. Shares	-	58,860	-	-	-	-	-
Issuance of Common Shares, Options	\$128	\$17	\$450	\$55	\$20	\$440	\$965
Issuance of Common Shares, PP	\$1,752	\$-	\$-	\$56,283	\$(179)	\$(313)	\$55,791
Warrants	\$-	\$-	\$-	\$1,018	\$-	\$-	\$1,018
Debt Financing	\$-	\$6,953	\$-	\$-	\$-	\$-	\$-
Repayment of debt	\$-	\$-	\$-	\$(7,814)	\$-	\$-	\$(7,814)
Deferred Financing Fees	(360)	(1,046)	(463)	463	-	-	-
Capital lease Payments	(4)	(7)	(2)	(2)	(3)	(2)	(9)
Cash Prov. By / (Used in) Fin. Act.	\$1,516	\$64,777	\$(15)	\$50,003	\$(162)	\$125	\$49,951
<b>Investing Activities</b>							
Short-term Investments	\$(4,310)	\$(20,067)	\$7,505	\$(20,030)	\$(122)	\$(15,120)	\$(27,767)
Acq. Of P&E	(626)	(4,425)	(913)	(501)	(219)	(382)	(2,015)
Acq. Of Intang. Assets	(227)	(1,039)	(3)	(28)	(1,051)	(24)	(1,106)
Cash Acq. From Kairos, Net	-	78	-	-	-	-	-
Acq. Of Equity Invest.	(4,038)	-	-	-	-	-	-
Cash Used in Investment Activities	\$(9,201)	\$(25,453)	\$6,589	\$(20,559)	\$(1,392)	\$(15,526)	\$(30,888)
Effect of FX on Cash & Cash Equiv.	(5,461)	840	132	58	37	-	227
Increase in Cash & Cash Equiv.	(35,316)	4,918	(5,991)	15,555	(13,669)	23,614	19,509
Cash & Equiv., Beginning of Period	46,835	11,519	16,437	10,446	26,001	12,332	16,437
Cash & Equiv., End of Period	\$11,519	\$16,437	\$10,446	\$26,001	\$12,332	\$35,946	\$35,946

Source: Zymeworks Inc., Raymond James Ltd.

## Appendix B: Select Management & Directors

### **Ali Tehrani, Ph.D., President, CEO, Director**

Dr. Tehrani is a co-founder of Zymeworks and currently serves as President and CEO. Dr. Tehrani has served as a member of the board of directors since the company's inception in September 2003. He holds a BSc and MSc from the University of Massachusetts and has a PhD from UBC. Dr. Tehrani is currently a member of the Board of Directors of LifeSciences BC, Creatus Biosciences Inc., CQDM and the BC Premier's Technology Council.

### **Neil Klompas, Chief Financial Officer**

Mr. Klompas joined Zymeworks Inc. in March 2007 and currently serves as CFO. Mr. Klompas brings over 20 years of healthcare and biotechnology experience. Prior to joining Zymeworks, he worked with KPMG LLP in Canada and the United States, most recently (from 2005 to 2007) with KPMG's Pharmaceuticals, Biotechnology and Medical Device M&A Transaction Services practice in Princeton, New Jersey. Prior to that, from 2000 to 2005 Mr. Klompas worked with KPMG's Canadian Biotechnology and Pharmaceuticals practice in the fields of assurance, valuations and taxation. Mr. Klompas is a CPA and is a member of the Chartered Professional Accountants of British Columbia. Mr. Klompas also holds a degree in Microbiology & Immunology from UBC and serves on the faculty advisory board for Biotechnology and Chemistry for Camosun College and as a Director for the Canadian Gene Cure Foundation and Ovensa Inc.

### **Diana Hausman, MD., Chief Medical Officer**

Dr. Hausman has served as Chief Medical Officer since June 2016. She is a board certified medical oncologist and brings more than 15 years of clinical drug development experience to the management team. Prior to joining Zymeworks Inc., she was Chief Medical Officer at Oncothyreon Inc. (now Cascadian Therapeutics, Inc.) from January 2012 to April 2016, where she oversaw the clinical program for their lead Phase 2 targeted anti-HER2 cancer therapy. While there, Dr. Hausman also led planning for the clinical development of a therapeutic vaccine, and earlier served as the company's Vice President, Clinical Development from September 2009 to December 2011. She has also held positions at ZymoGenetics, Inc., Berlex, Inc. and Immunex Corporation working across multiple indications, including oncology, hematology, hepatitis C and autoimmune disease. Dr. Hausman received her internal medicine training and specialty training in hematology and medical oncology at the University of Washington. She holds an M.D. degree from the University of Pennsylvania and an A.B. in biology from Princeton University.

### **Nick Bedford, Chairman**

Mr. Bedford has served as Chairman since September 2004. Previously, he served as Chairman of the Board of Directors of ActiveState Corporation, a software corporation, from May 2002 up to the time of its acquisition by Sophos Group plc in July 2003. Additionally, he has held senior positions at UBS Warburg from 1982 to 2002, including the Frankfurt-based role as Head of German Equities. Prior to this he was with UBS' Securities division in Zurich, Tokyo, and London. Mr. Bedford also currently serves on the Board of Actenum Corporation which he joined in 2003, and was previously a member of the board of Aegis Mobility from 2006 to January 2015. Mr. Bedford holds a B.Sc. in Civil Engineering from King's College, London University.

## Risks

### Financing Risk

Zymeworks has no commercial product revenues (aside from sporadic milestone payments), and is expected to continue to accumulate a loss from operations for the near term. Should market dynamics turn unfavorable resulting in Zymeworks losing access to capital in the public markets, there is risk of insolvency. Furthermore, we anticipate that Zymeworks will, from time to time, issue equity to raise capital, and thus investors should be aware of dilution risk.

### Competition Risk

Zymeworks is initially developing assets in what we believe to be one of the more competitive areas of drug development: oncology. There are a number of companies that are clinically advanced relative to Zymeworks, developing both HER2 targeted therapies as well as bispecific antibody therapeutics. Competition that could jeopardize Zymeworks ability to penetrate specific patient populations would materially impact the value of ZYME equity.

### Regulatory Risk

Currently Zymeworks has yet to have an asset reach the NDA/BLA phase of the regulatory process. We note that even if ZYME successfully completes all clinical trials leading up to a regulatory filing, there is no guarantee that their application will be approved.

### Pricing/Reimbursement Risk

While oncology drugs, and particularly orphan therapeutics have enjoyed a degree of pricing inelasticity, increased scrutiny on drug costs could impair Zymeworks' ability to command a pricing level in line with our estimates. Furthermore, the degree of flexibility in pricing ZW25/33 may be dependent on the level of efficacy demonstrated in its pivotal trials.

### Manufacturing Risk

As we have mentioned throughout our report, there is a large degree of variability in the reported prevalence of AA amyloidosis. We have relied on estimates generated by Navigent to derive our target patient population estimates. While we believe we have been conservative by taking the US median number and not accounting for RoW sales, there is no guarantee that Navigent's estimates will be proven accurate.

### Key Personnel Risk

We believe a critical differentiating aspect between ZYME and its competitors is the unique and differentiated skillsets held by its employees. We believe ZYME's future success depends on the technical and engineering expertise of its key employees, and loss of these employees could negatively alter ZYME's future development endeavors.

### IP Risk

Biotechnology is notorious for frequently litigious companies. Zymeworks may become involved in lawsuits to protect or enforce its patents and trade secrets, which could be expensive, time consuming and unsuccessful, negatively impacting ZYME shares.

**Company Citations**

Company Name	Ticker	Exchange	Currency	Closing Price	RJ Rating	RJ Entity
Asterias Biotherapeutics	AST	NYSE MKT	US\$	1.95	2	RJ & Associates
Celgene Corporation	CELG	NASDAQ	US\$	91.61	3	RJ & Associates
DSM	DSMN.AMS	AMS	€	79.90	1	RJEE/RJFI
Global Partners LP	GLP	NYSE	US\$	16.85	3	RJ & Associates
Johnson & Johnson	JNJ	NYSE	US\$	132.32	2	RJ & Associates
MEDNAX, Inc.	MD	NYSE	US\$	57.35	3	RJ & Associates
NantKwest, Inc.	NK	NASDAQ	US\$	4.17	3	RJ & Associates
Weyerhaeuser Company	WY	NYSE	US\$	35.24	1	RJ & Associates

Notes: Prices are as of the most recent close on the indicated exchange and may not be in US\$. See Disclosure section for rating definitions. Stocks that do not trade on a U.S. national exchange may not be registered for sale in all U.S. states. NC=not covered.

## IMPORTANT INVESTOR DISCLOSURES

Raymond James & Associates (RJA) is a FINRA member firm and is responsible for the preparation and distribution of research created in the United States. Raymond James & Associates is located at The Raymond James Financial Center, 880 Carillon Parkway, St. Petersburg, FL 33716, (727) 567-1000. Non-U.S. affiliates, which are not FINRA member firms, include the following entities which are responsible for the creation and distribution of research in their respective areas; In Canada, Raymond James Ltd. (RJL), Suite 2100, 925 West Georgia Street, Vancouver, BC V6C 3L2, (604) 659-8200; In Europe, Raymond James Euro Equities, SAS, 40, rue La Boetie, 75008, Paris, France, +33 1 45 61 64 90, and Raymond James Financial International Ltd., Broadwalk House, 5 Appold Street, London, England EC2A 2AG, +44 203 798 5600.

This document is not directed to, or intended for distribution to or use by, any person or entity that is a citizen or resident of or located in any locality, state, country, or other jurisdiction where such distribution, publication, availability or use would be contrary to law or regulation. The securities discussed in this document may not be eligible for sale in some jurisdictions. This research is not an offer to sell or the solicitation of an offer to buy any security in any jurisdiction where such an offer or solicitation would be illegal. It does not constitute a personal recommendation nor does it take into account the particular investment objectives, financial situations, or needs of individual clients. Information in this report should not be construed as advice designed to meet the individual objectives of any particular investor. **Investors should consider this report as only a single factor in making their investment decision.** Consultation with your investment advisor is recommended. Past performance is not a guide to future performance, future returns are not guaranteed, and a loss of original capital may occur.

The information provided is as of the date above and subject to change, and it should not be deemed a recommendation to buy or sell any security. Certain information has been obtained from third-party sources we consider reliable, but we do not guarantee that such information is accurate or complete. Persons within the Raymond James family of companies may have information that is not available to the contributors of the information contained in this publication. Raymond James, including affiliates and employees, may execute transactions in the securities listed in this publication that may not be consistent with the ratings appearing in this publication.

With respect to materials prepared by Raymond James Ltd. ("RJL"), all expressions of opinion reflect the judgment of the Research Department of RJL, or its affiliates, at this date and are subject to change. RJL may perform investment banking or other services for, or solicit investment banking business from, any company mentioned in this document.

Raymond James ("RJ") research reports are disseminated and available to RJ's retail and institutional clients simultaneously via electronic publication to RJ's internal proprietary websites ([RJ Investor Access](#) & [RJ Capital Markets](#)). Not all research reports are directly distributed to clients or third-party aggregators. Certain research reports may only be disseminated on RJ's internal proprietary websites; however such research reports will not contain estimates or changes to earnings forecasts, target price, valuation, or investment or suitability rating. Individual Research Analysts may also opt to circulate published research to one or more clients electronically. This electronic communication distribution is discretionary and is done only after the research has been publically disseminated via RJ's internal proprietary websites. The level and types of communications provided by Research Analysts to clients may vary depending on various factors including, but not limited to, the client's individual preference as to the frequency and manner of receiving communications from Research Analysts. For research reports, models, or other data available on a particular security, please contact your RJ Sales Representative or visit [RJ Investor Access](#) or [RJ Capital Markets](#).

Links to third-party websites are being provided for information purposes only. Raymond James is not affiliated with and does not endorse, authorize, or sponsor any of the listed websites or their respective sponsors. Raymond James is not responsible for the content of any third-party website or the collection or use of information regarding any website's users and/or members.

In the event that this is a compendium report (i.e., covers 6 or more subject companies), Raymond James Ltd. may choose to provide specific disclosures for the subject companies by reference. To access these disclosures, clients should refer to: <http://www.raymondjames.ca> (click on Equity Capital Markets / Equity Research / Research Disclosures) or call toll-free at 1-800-667-2899.

---

## ANALYST INFORMATION

**Analyst Compensation:** Equity research analysts and associates at Raymond James are compensated on a salary and bonus system. Several factors enter into the compensation determination for an analyst, including i) research quality and overall productivity, including success in rating stocks on an absolute basis and relative to the local exchange composite Index and/or a sector index, ii) recognition from institutional investors, iii) support effectiveness to the institutional and retail sales forces and traders, iv) commissions generated in stocks under coverage that are attributable to the analyst's efforts, v) net revenues of the overall Equity Capital Markets Group, and vi) compensation levels for analysts at competing investment dealers.

The views expressed in this report accurately reflect the personal views of the analyst(s) covering the subject securities. No part of said person's compensation was, is, or will be directly or indirectly related to the specific recommendations or views contained in this research report. In addition, said analyst has not received compensation from any subject company in the last 12 months.

## RATINGS AND DEFINITIONS

**Raymond James Ltd. (Canada) definitions:** Strong Buy (SB1) The stock is expected to appreciate and produce a total return of at least 15% and outperform the S&P/TSX Composite Index over the next six months. Outperform (MO2) The stock is expected to appreciate and outperform the S&P/TSX Composite Index over the next twelve months. Market Perform (MP3) The stock is expected to perform generally in line with the S&P/TSX Composite Index over the next twelve months and is potentially a source of funds for more highly rated securities. Underperform (MU4) The stock is expected to underperform the S&P/TSX Composite Index or its sector over the next six to twelve months and should be sold.

**Raymond James & Associates (U.S.) definitions:** Strong Buy (SB1) Expected to appreciate, produce a total return of at least 15%, and outperform the S&P 500 over the next six to 12 months. For higher yielding and more conservative equities, such as REITs and certain MLPs, a total return of at least 15% is expected to be realized over the next 12 months. Outperform (MO2) Expected to appreciate and outperform the S&P 500 over the next 12-18 months. For higher yielding and more conservative equities, such as REITs and certain MLPs, an Outperform rating is used for securities where we are comfortable with the relative safety of the dividend and expect a total return modestly exceeding the dividend yield over the next 12-18 months. Market Perform (MP3) Expected to perform generally in line with the S&P 500 over the next 12 months. Underperform (MU4) Expected to underperform the S&P 500 or its sector over the next six to 12 months and should be sold. Suspended (S) The rating and price target have been suspended temporarily. This action may be due to market events that made coverage impracticable, or to comply with applicable regulations or firm policies in certain circumstances, including when Raymond James may be providing investment banking services to the company. The previous rating and price target are no longer in effect for this security and should not be relied upon.

**Raymond James Europe (Raymond James Euro Equities SAS & Raymond James Financial International Limited) rating definitions:** Strong Buy (1) Expected to appreciate, produce a total return of at least 15%, and outperform the Stoxx 600 over the next 6 to 12 months. Outperform (2) Expected to appreciate and outperform the Stoxx 600 over the next 12 months. Market Perform (3) Expected to perform generally in line with the Stoxx 600 over the next 12 months. Underperform (4) Expected to underperform the Stoxx 600 or its sector over the next 6 to 12 months. Suspended (S) The rating and target price have been suspended temporarily. This action may be due to market events that made coverage impracticable, or to comply with applicable regulations or firm policies in certain circumstances, including when Raymond James may be providing investment banking services to the company. The previous rating and target price are no longer in effect for this security and should not be relied upon.

In transacting in any security, investors should be aware that other securities in the Raymond James research coverage universe might carry a higher or lower rating. Investors should feel free to contact their Financial Advisor to discuss the merits of other available investments.

### Suitability Ratings (SR)

**Medium Risk/Income (M/INC)** Lower to average risk equities of companies with sound financials, consistent earnings, and dividend yields above that of the S&P 500. Many securities in this category are structured with a focus on providing a consistent dividend or return of capital.

**Medium Risk/Growth (M/GRW)** Lower to average risk equities of companies with sound financials, consistent earnings growth, the potential for long-term price appreciation, a potential dividend yield, and/or share repurchase program.

**High Risk/Income (H/INC)** Medium to higher risk equities of companies that are structured with a focus on providing a meaningful dividend but may face less predictable earnings (or losses), more leveraged balance sheets, rapidly changing market dynamics, financial and competitive issues, higher price volatility (beta), and potential risk of principal. Securities of companies in this category may have a less predictable income stream from dividends or distributions of capital.

**High Risk/Growth (H/GRW)** Medium to higher risk equities of companies in fast growing and competitive industries, with less predictable earnings (or losses), more leveraged balance sheets, rapidly changing market dynamics, financial or legal issues, higher price volatility (beta), and potential risk of principal.

**High Risk/Speculation (H/SPEC)** High risk equities of companies with a short or unprofitable operating history, limited or less predictable revenues, very high risk associated with success, significant financial or legal issues, or a substantial risk/loss of principal.

Note that Raymond James Ltd. (RJL) has developed a proprietary algorithm for risk rating individual securities. The algorithm utilizes data from multiple vendors, and all data is refreshed at least monthly. Accordingly, Suitability Ratings are updated monthly. The Suitability Rating shown on this report is current as of the report's published date. In the event that a Suitability Rating changes after the published date, the new rating will not be reflected in research materials until the analyst publishes a subsequent report.

## RATING DISTRIBUTIONS

	Coverage Universe Rating Distribution*			Investment Banking Distribution		
	RJL	RJA	RJEE/RJFI	RJL	RJA	RJEE/RJFI
<b>Strong Buy and Outperform (Buy)</b>	68%	54%	51%	40%	23%	0%
<b>Market Perform (Hold)</b>	28%	41%	34%	23%	12%	0%
<b>Underperform (Sell)</b>	4%	5%	15%	25%	7%	0%

\* Columns may not add to 100% due to rounding.

## RAYMOND JAMES RELATIONSHIP DISCLOSURES

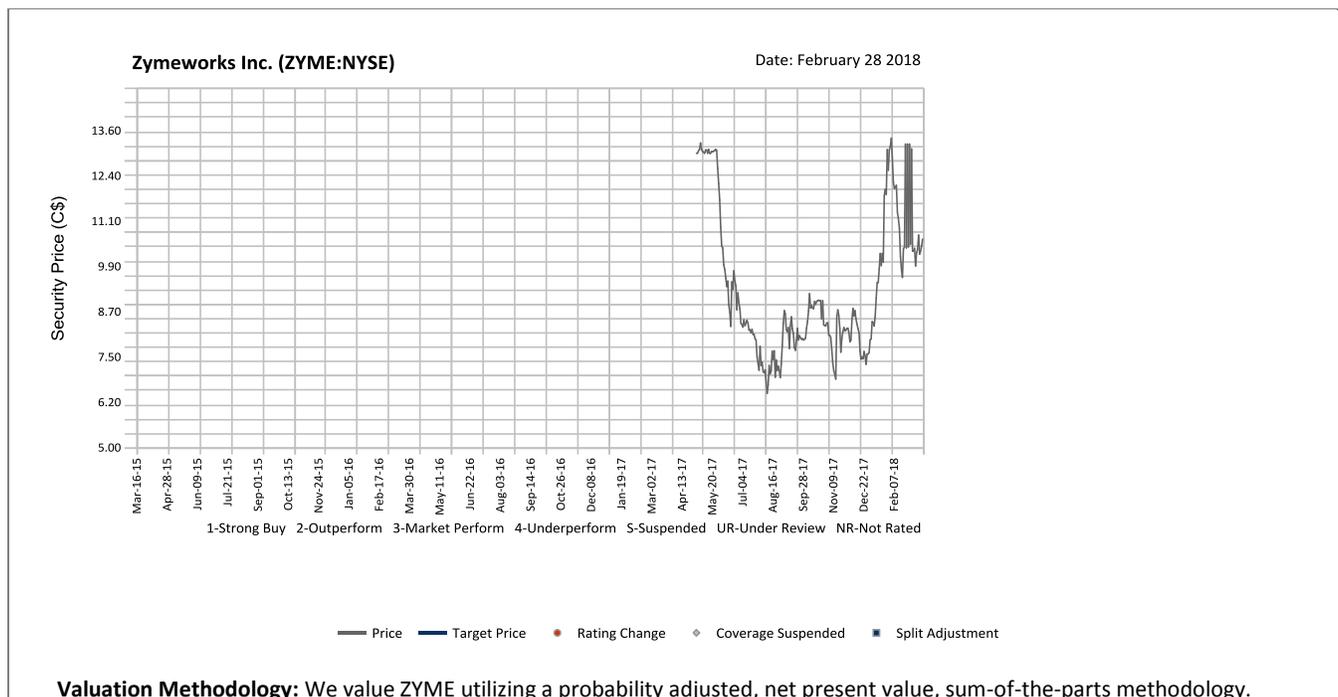
Raymond James Ltd. or its affiliates expects to receive or intends to seek compensation for investment banking services from all companies under research coverage within the next three months.

Company Name	Disclosure
Zymeworks Inc.	The Analyst and/or Associate or a member of his/their household has a long position in the securities of ZYME. Raymond James Ltd - the analyst and/or associate has viewed the material operations of ZYME.

## STOCK CHARTS, TARGET PRICES, AND VALUATION METHODOLOGIES

**Valuation Methodology:** The Raymond James methodology for assigning ratings and target prices includes a number of qualitative and quantitative factors including an assessment of industry size, structure, business trends and overall attractiveness; management effectiveness; competition; visibility; financial condition, and expected total return, among other factors. These factors are subject to change depending on overall economic conditions or industry- or company-specific occurrences.

**Target Prices:** The information below indicates our target price and rating changes for ZYME stock over the past three years.



## RISK FACTORS

**General Risk Factors:** Following are some general risk factors that pertain to the businesses of the subject companies and the projected target prices and recommendations included on Raymond James research: (1) Industry fundamentals with respect to customer demand or product / service pricing could change and adversely impact expected revenues and earnings; (2) Issues relating to major competitors or market shares or new product expectations could change investor attitudes toward the sector or this stock; (3) Unforeseen

developments with respect to the management, financial condition or accounting policies or practices could alter the prospective valuation.

#### **Risks - Zymeworks Inc.**

##### **Financing Risk**

Zymeworks has no commercial product revenues (aside from sporadic milestone payments), and is expected to continue to accumulate a loss from operations for the near term. Should market dynamics turn unfavorable resulting in Zymeworks losing access to capital in the public markets, there is risk of insolvency. Furthermore, we anticipate that Zymeworks will, from time to time, issue equity to raise capital, and thus investors should be aware of dilution risk.

##### **Competition Risk**

Zymeworks is initially developing assets in what we believe to be one of the more competitive areas of drug development: oncology. There are a number of companies that are clinically advanced relative to Zymeworks, developing both HER2 targeted therapies as well as bispecific antibody therapeutics. Competition that could jeopardize Zymeworks ability to penetrate specific patient populations would materially impact the value of ZYME equity.

##### **Regulatory Risk**

Currently Zymeworks has yet to have an asset reach the NDA/BLA phase of the regulatory process. We note that even if ZYME successfully completes all clinical trials leading up to a regulatory filing, there is no guarantee that their application will be approved.

##### **Pricing/Reimbursement Risk**

While oncology drugs, and particularly orphan therapeutics have enjoyed a degree of pricing inelasticity, increased scrutiny on drug costs could impair Zymeworks' ability to command a pricing level in line with our estimates. Furthermore, the degree of flexibility in pricing ZW25/33 may be dependent on the level of efficacy demonstrated in its pivotal trials.

##### **Manufacturing Risk**

As we have mentioned throughout our report, there is a large degree of variability in the reported prevalence of AA amyloidosis. We have relied on estimates generated by Navigent to derive our target patient population estimates. While we believe we have been conservative by taking the US median number and not accounting for RoW sales, there is no guarantee that Navigent's estimates will be proven accurate.

##### **Key Personnel Risk**

We believe a critical differentiating aspect between ZYME and its competitors is the unique and differentiated skillsets held by its employees. We believe ZYME's future success depends on the technical and engineering expertise of its key employees, and loss of these employees could negatively alter ZYME's future development endeavors.

##### **IP Risk**

Biotechnology is notorious for frequently litigious companies. Zymeworks may become involved in lawsuits to protect or enforce its patents and trade secrets, which could be expensive, time consuming and unsuccessful, negatively impacting ZYME shares.

**Additional Risk and Disclosure information, as well as more information on the Raymond James rating system and suitability categories, is available for Raymond James at [rjcapitalmarkets.com/Disclosures/index](http://rjcapitalmarkets.com/Disclosures/index) and for Raymond James Limited at [www.raymondjames.ca/researchdisclosures](http://www.raymondjames.ca/researchdisclosures).**

## **INTERNATIONAL DISCLOSURES**

### **FOR CLIENTS IN THE UNITED STATES:**

Any foreign securities discussed in this report are generally not eligible for sale in the U.S. unless they are listed on a U.S. exchange. This report is being provided to you for informational purposes only and does not represent a solicitation for the purchase or sale of a security in any state where such a solicitation would be illegal. Investing in securities of issuers organized outside of the U.S., including ADRs, may entail certain risks. The securities of non-U.S. issuers may not be registered with, nor be subject to the reporting requirements of, the U.S. Securities and Exchange Commission. There may be limited information available on such securities. Investors who have received this report may be prohibited in certain states or other jurisdictions from purchasing the securities mentioned in this report. Please ask your Financial Advisor for additional details and to determine if a particular security is eligible for purchase in your state.

Raymond James Ltd. is not a U.S. broker-dealer and therefore is not governed by U.S. laws, rules or regulations applicable to U.S. broker-dealers. Consequently, the persons responsible for the content of this publication are not licensed in the U.S. as research analysts in accordance with applicable rules promulgated by the U.S. Self Regulatory Organizations.

Any U.S. Institutional Investor wishing to effect trades in any security should contact Raymond James (USA) Ltd., a U.S. broker-dealer affiliate of Raymond James Ltd.

**FOR CLIENTS IN THE UNITED KINGDOM:**

**For clients of Raymond James Financial International Limited (RJFI):** This document and any investment to which this document relates is intended for the sole use of the persons to whom it is addressed, being persons who are Eligible Counterparties or Professional Clients as described in the FCA rules or persons described in Articles 19(5) (Investment professionals) or 49(2) (High net worth companies, unincorporated associations etc) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended) or any other person to whom this promotion may lawfully be directed. It is not intended to be distributed or passed on, directly or indirectly, to any other class of persons and may not be relied upon by such persons and is therefore not intended for private individuals or those who would be classified as Retail Clients.

**For clients of Raymond James Investment Services, Ltd.:** This report is for the use of professional investment advisers and managers and is not intended for use by clients.

For purposes of the Financial Conduct Authority requirements, this research report is classified as independent with respect to conflict of interest management. RJFI, and Raymond James Investment Services, Ltd. are authorised and regulated by the Financial Conduct Authority in the United Kingdom.

**FOR CLIENTS IN FRANCE:**

This document and any investment to which this document relates is intended for the sole use of the persons to whom it is addressed, being persons who are Eligible Counterparties or Professional Clients as described in “Code Monétaire et Financier” and Règlement Général de l’Autorité des Marchés Financiers. It is not intended to be distributed or passed on, directly or indirectly, to any other class of persons and may not be relied upon by such persons and is therefore not intended for private individuals or those who would be classified as Retail Clients.

**For clients of Raymond James Euro Equities:** Raymond James Euro Equities is authorised and regulated by the Autorité de Contrôle Prudentiel et de Résolution and the Autorité des Marchés Financiers.

**For institutional clients in the European Economic Area (EEA) outside of the United Kingdom:** This document (and any attachments or exhibits hereto) is intended only for EEA institutional clients or others to whom it may lawfully be submitted.

---

**Proprietary Rights Notice:** By accepting a copy of this report, you acknowledge and agree as follows:

This report is provided to clients of Raymond James only for your personal, noncommercial use. Except as expressly authorized by Raymond James, you may not copy, reproduce, transmit, sell, display, distribute, publish, broadcast, circulate, modify, disseminate or commercially exploit the information contained in this report, in printed, electronic or any other form, in any manner, without the prior express written consent of Raymond James. You also agree not to use the information provided in this report for any unlawful purpose.

This report and its contents are the property of Raymond James and are protected by applicable copyright, trade secret or other intellectual property laws (of the United States and other countries). United States law, 17 U.S.C. Sec.501 et seq, provides for civil and criminal penalties for copyright infringement. No copyright claimed in incorporated U.S. government works.

Additional information is available upon request. This document may not be reprinted without permission.

RJL is a member of the Canadian Investor Protection Fund. ©2018 Raymond James Ltd.

## RAYMOND JAMES LTD. CANADIAN INSTITUTIONAL EQUITY TEAM WWW.RAYMONDJAMES.CA

## EQUITY RESEARCH

HEAD OF EQUITY RESEARCH  
DARYL SWETLISHOFF, CFA 604.659.8246

## CONSUMER

CONSUMER & RETAIL  
KENRIC TYGHE, MBA 416.777.7188  
JOANNA CHMIEL (ASSOCIATE) 416.777.7060

## ENERGY

OIL & GAS ENERGY SERVICES, HEAD OF ENERGY RESEARCH  
ANDREW BRADFORD, CFA 403.509.0503  
MICHAEL SHAW, CFA (SR ASSOCIATE) 403.509.0534  
VICTOR EL-ARAJ (JR ASSOCIATE) 403.221.0377

## OIL &amp; GAS PRODUCERS

KURT MOLNAR 403.221.0414  
GORDON STEPPAN, CFA (SR ASSOCIATE) 403.221.0411

## OIL &amp; GAS PRODUCERS

JEREMY MCCREA, CFA 403.509.0518  
RAHUL PANDEY (ASSOCIATE) 403.509.0521

## SR. OIL &amp; GAS PRODUCERS | ENERGY INFRASTRUCTURE

CHRIS COX, CFA 416.777.7175  
GEORGE HUANG (ASSOCIATE) 416.777.7180

## POWER &amp; UTILITIES

DAVID QUEZADA, CFA 604.659.8257

## FINANCIAL SERVICES

DIVERSIFIED FINANCIALS  
BRENNAN PHELAN, CFA, CPA, CA 416.777.7042

## FOREST PRODUCTS

FOREST PRODUCTS  
DARYL SWETLISHOFF, CFA 604.659.8246  
BRYAN FAST, CFA (SR ASSOCIATE) 604.659.8262

## HEALTHCARE

BIOTECHNOLOGY, HEALTHCARE  
DAVID NOVAK 416.777.7029

## INDUSTRIAL &amp; TRANSPORTATION

INDUSTRIAL | TRANSPORTATION, HEAD OF INDUSTRIAL RESEARCH  
BEN CHERNIAVSKY 604.659.8244  
MARK BEGERT (ASSOCIATE) 604.659.8380

## INFRASTRUCTURE &amp; CONSTRUCTION

FREDERIC BASTIEN, CFA 604.659.8232  
MATT BORYS (ASSOCIATE) 604.654.1236

## TRANSPORTATION | CHEMICALS &amp; AGRIBUSINESS

STEVE HANSEN, CFA, CPA, CMA 604.659.8208  
KANISH PAWAR (ASSOCIATE) 604.659.8238

## MINING

BASE & PRECIOUS METALS, HEAD OF MINING RESEARCH  
BRIAN MACARTHUR, CFA 416.777.4914  
CHRIS LAW (ASSOCIATE) 416.777.7144

## BASE &amp; PRECIOUS METALS

FAROOQ HAMED, CA 416.777.7117  
BRANDON THROOP (SR ASSOCIATE) 416.777.7165

## PRECIOUS METALS

TARA HASSAN, P.ENG 604.659.8064  
JEREMY POON (ASSOCIATE) 604.659.8294

## REAL ESTATE

REAL ESTATE & REITS  
KEN AVALOS, MBA 727.567.1756  
JOHANN RODRIGUES 416.777.7189

## TECHNOLOGY &amp; COMMUNICATIONS

TECHNOLOGY  
STEVEN LI, CFA 416.777.4918  
ANSHU DEORA (ASSOCIATE) 416.777.6414

## EQUITY RESEARCH PUBLISHING

SENIOR SUPERVISORY ANALYST  
HEATHER HERRON 403.509.0509  
HEAD OF PUBLISHING | SUPERVISORY ANALYST  
CYNTHIA LUI 604.659.8210  
TYLER BOS (SUPERVISORY ANALYST | EDITOR) 647.624.1596  
INDER GILL (RESEARCH EDITOR) 604.659.8202  
KATE MAJOR (RESEARCH PRINCIPAL | EDITOR) 416.777.7173  
ASHLEY RAMSAY (SUPERVISORY ANALYST | EDITOR) 604.376.2291

## INSTITUTIONAL EQUITY SALES

HEAD OF SALES  
MIKE WESTCOTT 416.777.4935  
MICHELLE MARGUET (ECM, INSTITUTIONAL MARKETING) 416.777.4951

## TORONTO (CAN 1.888.601.6105 | USA 1.800.290.4847)

SEAN BOYLE 416.777.4927  
JEFF CARRUTHERS, CFA 416.777.4929  
RICHARD EAKINS 416.777.4926  
JONATHAN GREER 416.777.4930  
DAVE MACLENNAN 416.777.4934  
ROBERT MILLS, CFA 416.777.4945  
BRADY PIMLOTT 416.777.4993  
NICOLE SVEC-GRIFFIS, CFA (U.S. EQUITIES) 416.777.4942  
NEIL WEBER 416.777.4931  
ORNELLA BURNS (ASSISTANT) 416.777.4928  
SATBIR CHATRATH (ASSISTANT, CURRENTLY ON LEAVE) 416.777.4915  
JILLIAN STOLTZ (ASSISTANT) 416.777.4915

## VANCOUVER (1.800.667.2899)

SCOT ATKINSON, CFA 604.659.8225  
NICK POCRNIC 604.659.8230  
TERRI MCEWAN (ASSISTANT) 604.659.8228

## MONTREAL (514.350.4450 | 1.866.350.4455)

JOHN HART 514.350.4462  
DAVID MAISLIN, CFA 514.350.4460  
TANYA HATCHER (ASSISTANT) 514.350.4458

## LONDON

ADAM WOOD 0.207.426.5612

## INSTITUTIONAL EQUITY TRADING

CO-HEAD OF TRADING  
BOB McDONALD, CFA 604.659.8222  
ANDREW FOOTE, CFA 416.777.4924

## TORONTO (CANADA 1.888.601.6105 | USA 1.800.290.4847)

MARK ARMSTRONG 416.777.4981  
PAM BANKS 416.777.4923  
OLIVER HERBST 416.777.4947  
ANDY HERRMANN 416.777.4937  
MATT MALOWNEY 416.777.4941  
ERIC MUNRO, CFA 416.777.4983  
BOB STANDING 416.777.4921  
PETER MASON (ASSISTANT) 416.777.7195

## VANCOUVER (1.800.667.2899)

NAV CHEEMA 604.659.8224  
FRASER JEFFERSON 604.659.8218  
DEREK ORAM 604.659.8223

## MONTREAL (514.350.4450 | 1.866.350.4455)

JOE CLEMENT 514.350.4470  
PATRICK SANCHE 514.350.4465

## INSTITUTIONAL EQUITY OFFICES

Calgary	Montreal	Vancouver
Suite 4250	Suite 3000	Suite 2100
525 8th Avenue SW	1800 McGill College	925 West Georgia Street
Calgary, AB T2P 1G1	Montreal, PQ H3A 3J6	Vancouver, BC V6C 3L2
403.509.0500	514.350.4450	604.659.8000
	Toll Free: 1.866.350.4455	Toll Free: 1.800.667.2899

## Toronto

Suite 5400, Scotia Plaza 40 King Street West  
Toronto, ON M5H 3Y2  
416.777.4900  
Toll Free Canada: .888.601.6105  
Toll Free USA: 1.800.290.4847

## International Headquarters

The Raymond James Financial Center  
880 Carillon Parkway  
St. Petersburg, FL  
USA 33716  
727.567.1000