



DIVISION OF
CORPORATION FINANCE

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

Mail Stop 4546

January 10, 2017

Dr. Ali Tehrani
President and Chief Executive
Zymeworks Inc.
Suite 540—1385 West 8th Avenue
Vancouver, BC V6H 3V9
Canada

**Re: Zymeworks Inc.
Draft Registration Statement on Form F-1
Submitted December 13, 2016
CIK No. 0001403752**

Dear Dr. Tehrani:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Summary
Overview, page 1

1. Please clarify the meaning of any significant scientific or technical terms the first time they are used in order to ensure that lay readers will understand the disclosure. For example, please briefly explain what you mean by “bispecific antibody,” “cytotoxic payload,” “epitope,” “Fab,” “linker,” “multivalent scaffolds,” “PFS,” “OS,” “cytotoxic drug conjugation,” and “multivalent targeting” at their first use. Please also explain what you mean by an “adaptive” Phase 1 clinical trial. In addition, please explain the competitive advantage listed in the third bullet point relating to Native (IgG or HAS) Formats so that a lay reader may understand its significance.

2. We note your statements here and throughout the prospectus regarding the “safety and efficacy” of your product candidates, such as your “multiple wholly-owned product candidates that demonstrate safety and efficacy,” your “lead product candidates have demonstrated a favorable safety profile,” your platform includes “optimized efficacy and safety profiles” your biotherapeutics will “result in superior safety, efficacy and patient outcomes,” ZymeLink-cytotoxin conjugates “demonstrate exceptional anti-tumor efficacy and tolerability,” and “preclinical studies demonstrate that ZW25 is efficacious against breast tumors....” Because approval of the FDA is dependent on it making a determination that a drug or biologic is effective, it is premature for you to describe your technology or product candidates as safe and effective. Please revise these statements in your prospectus accordingly.
3. You state that your product candidates demonstrate “enhanced safety and efficacy with the potential to drive superior outcomes in large underserved and unaddressed patient populations.” In addition to revising the language about safety and efficacy, please explain how your product candidates are “enhanced,” including what you are using as a comparison for your candidates. Please also clarify the particular underserved and unaddressed population to which you refer.
4. We note your disclosure here and in your Business section that your therapeutic platforms have been validated through strategic partnerships with various pharmaceutical companies. Please revise your disclosure to make clear that the strategic partnerships only involve your Azymetric and EFECT platforms. Please also clearly state, to the extent accurate, that these platforms are being used by the strategic partners for their own development.
5. Please disclose the amount of your accumulated deficit.

Our Pipeline of Product Candidates, page 5

6. We note your statement that there is a “substantial population” of patients whose tumors express lower levels of validated targets. Please quantify, to the extent practicable, what you mean by “substantial” and whether this population may receive other treatments or therapies aside from those you discuss here.
7. Please revise your product pipeline table here and in the Business section to remove the programs that are in the discovery phase. Because you have not identified a product candidate for these programs, it is premature to include them in a product pipeline table.

Implications of Being an Emerging Growth Company, page 7

8. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your

behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

Use of Proceeds, page 64

9. Please revise your disclosure regarding the first two uses to explain what stage of development you expect to reach with the allocated amount (*e.g.*, through the Phase 2 trial or through the filing of a NDA). If the anticipated proceeds will not be sufficient to fund each of the listed uses, please disclose the amount and sources of other funds needed. See Item 3.C.1. of Form 20-F.
10. Please reconcile your planned use of offering proceeds for the clinical development of ZW25 and ZW33 with your disclosure on page 92 that your existing cash and cash equivalents and short term investments as of September 30, 2016, combined with collaboration payments, will enable you to fund the clinical development of these product candidates.
11. Please identify whether any material part of the proceeds will be used to discharge, reduce or retire indebtedness. If so, please provide the information required by Item 3.C.4. of Form 20-F.

Management's Discussion and Analysis of Financial Condition and Results of Operations

Critical Accounting Policies and Significant Judgments and Estimates

Share-Based Compensation, page 83

12. Please disclose the methods that management used to determine the fair value of the company's shares and the nature of the material assumptions involved. Tell us what events resulted in the decrease of the estimated fair value between the October 1, 2015 and January 1, 2016 valuation dates and what events resulted in the increase of the estimated fair value between the February 29, 2016 and November 9, 2016 valuation dates. Confirm for us that the methods and the nature of material assumptions used to arrive at the fair values at the dates herein were the same as those used to determine the fair value for your common stock issued in the Kairos acquisition. If not, please explain. Also explain the events that resulted in the increase of the estimated fair value between the February 29, 2016 and the March 18, 2016 (Kairos acquisition date) valuation dates.
13. Once you have an estimated offering price or range, please explain to us the reasons for any differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock compensation and beneficial conversion features.

14. Please revise your tabular disclosures on pages 84, 85, 184 and elsewhere as applicable to also reflect amounts in U.S. dollars.

Financial Operations Overview

Research and Development Expense, page 78

15. Please tell us the amount and nature of costs incurred for each period presented for prosecuting and maintaining intellectual property directly related to your product candidates and therapeutic platforms. Tell us how each cost qualifies as research or development as defined in ASC 730-10-20 and discussed in ASC 730-10-55-1 and 55-2.
16. Indicate, for each period presented, how much of your research and development expense represents costs incurred related to your collaboration and licensing agreements. Discuss the reasons for period over period fluctuations of these costs in the results of operations sections.

Liquidity and Capital Resources, page 90

17. Please disclose the specific milestones you must achieve to be eligible for the Tranche B Term Loan under the Perceptive Facility.

Funding Requirements, page 91

18. Please quantify by collaborator and agreement the collaboration payments along with their nature and timing that you anticipate receiving that will enable you to fund the clinical development of ZW25 and ZW33 product candidates based on your Azymetric platform technology. Disclose the basis for your assumption that all of your strategic partners' programs will advance as currently contemplated. Provide similar disclosure, as applicable, on page 125 in the first paragraph under "Our Strategic Partnerships."

Business

Overview, page 94

19. We note your statement here and elsewhere that 81% of patients with HER2-expressing breast cancer and 57% of patients with HER2-expressing gastric and gastroesophageal cancer have low to intermediate levels of HER2 and are ineligible for HER2-targeted therapies. So that investors may better understand your market opportunity, please disclose whether there are alternative treatments or therapies available for patients with low to intermediate levels of HER2 and whether such patients have similar survival and relapse rates as patients that are HER2 high-expressing. To the extent such patients receive alternative treatments or therapies, please explain how this is a significant unmet need.

Azymetric Bispecific Antibody Platform, page 96

20. Please revise your disclosure to explain what it means that the “dual-targeting of Azymetric antibodies has demonstrated synergistic efficacy in preclinical studies.”

Our Strategy, page 98

21. We note that you plan to “aggressively advance” ZW25 through clinical trials, and plan to discuss “accelerated registration paths” if data in your trials is “highly compelling.” We further note your statement that you will be able to realize significant cost and time savings for ZW25 and ZW33 because they share an identical bispecific antibody backbone. Please tell us why you believe your product candidates may have an accelerated timeline for clinical trials as compared to other product candidates. In particular we note that ZW25 is just starting Phase 1 and ZW33 is still preclinical, therefore it is unclear how you will be able to realize significant cost and time savings. Please also revise your disclosure in this section as appropriate.

ZymeLink Conjugation Platform and Cytotoxins, page 108

22. Please further expand your disclosure on pages 108 and 109 to explain the studies that resulted in the findings presented here, including when you conducted the studies and over what period of time, as well as the significance of the graphs. In your disclosure, please explain why ZymeLink was compared to MMAE and if Trastuzumab-MMAE is the only other “currently approved ADC approach.” If not, please explain how you concluded that ZymeLink cytotoxin-conjugates are tolerated by non-human primates at doses several-fold higher than currently approved ADC approaches. In addition, please explain how ZymeLink ADCs exhibit “superior pharmacokinetic properties” than other ADCs.

EFECT Antibody Effector Function Modulation Platform, page 110

23. Please revise this section to describe the EFECT platform so that a lay investor may understand the disclosure. The purpose and general description of the EFECT platform, EFECT variants, and the graphs on page 111 are unclear.

Preclinical Development of ZW25, page 118

24. Please explain the significance of hIgG in this study. Please also explain why ZW25 was not compared to trastuzumab in the ovarian cancer model and also make clear that these studies were done using mice. Please include similar disclosure in the ZW33 preclinical studies discussed on pages 122-124, as appropriate.

25. At your first use of the term “statistically significant” on page 119, please provide an explanation of the term and discuss how statistical significance relates to the FDA’s evidentiary standards of efficacy.
26. Please disclose the indications that are included for the IND application filed for ZW25.

Potential Advantages of ZW33, page 122

27. We note your statement that the “potential for increased efficiency should allow ZW33 to replace Kadcyla as the preferred therapy for second line treatment of HER2+ metastatic cancer.” Given that ZW33 is in pre-clinical development, this statement appears to be premature. Please remove this disclosure or tell us why you believe it is appropriate.
28. We refer to your statement in the penultimate paragraph on page 124 that in general, adverse effects reported for ZW33 at certain doses were similar to those reported for corresponding doses of DM1 or T-DM1. Please describe the reported adverse effects for ZW33.

Strategic Partnerships and Collaborations, page 125

29. Please clarify in this section, as appropriate, that the biospecific antibodies generated through the strategic partnerships and collaborations are for the development of the strategic partners and you will not have ownership of any of such antibodies.
30. Please revise your disclosure in this section regarding your agreements with your strategic partners to break down the amount you will receive for the research, development and commercial milestones individually. Please also specify the duration of the royalty payments for each agreement. In addition, regarding your GSK (2015) agreement, please clarify when the research period ends.
31. Please disclose the minimum cash balance that you must maintain under the Lilly (2014) agreement.
32. Please revise your disclosure regarding the royalty rates applicable to the Daiichi agreement to quantify them within a ten point range.

Intellectual Property, page 130

33. We refer to your statement that two of your patent families are co-owned with VAR2 Pharmaceuticals ApS. Please expand your disclosure to explain which of your patents are co-owned, and whether there is any agreement between you and VAR2 covering the patents. If you have an agreement, please disclose all material terms of such agreement and file it as an exhibit to the registration statement.

34. Please revise your disclosure to describe the material terms of your agreements with CDRD Ventures, ITS, NRC, Selexis and ProBioGen described on page 132 and file these agreements as exhibits to your registration statement. In the alternative, please tell us why such disclosure is not required.

Executive Compensation

Executive Employment Arrangements . . . , page 168

35. Please revise your disclosure in this section to present the compensation disclosure for the year ended December 31, 2016, the company's last full financial year. See Item 6.B. of Form 20-F.
36. We refer to your table on page 169, which appears to show amounts in Canadian dollars, and footnote 1, which states that the reported amounts have been converted to U.S. dollars. Please reconcile these disclosures.

Principal Shareholders, page 175

37. Please revise your disclosure to identify the natural person(s) who have voting and investment control of the shares held by CTI Life Sciences Fund, L.P. and Celgene Alpine Investment Co.
38. Please include the information required by Item 7.A.2. of Form 20-F.

Consolidated Financial Statements

Notes to Consolidated Financial Statements

5. Equity Investment and Acquisition of Kairos, page F-19

39. Please tell us why the cost approach to estimate the fair value of acquired IPR&D for each project is appropriate. Tell us more specifically the mechanics regarding your application of the cost approach to estimate, for each project, "total research costs incurred to date in order to recreate the asset, estimated cost multiples from comparable companies and expected investor return rates." Provide us a schedule by project of the acquisition date fair values.

11. Redeemable Convertible Class A Preferred Shares, Special Shares and Shareholders' Equity, page F-25

40. Substantiate for us the expected volatility rates you use throughout this note.

13. Research Collaboration and Licensing Agreements, page F-32

41. Please present the expense incurred by agreement for each period presented and indicate where the amounts are included within the consolidated statements of loss and comprehensive loss.
42. Please revise your disclosure to clarify how your revenue recognition policy disclosed on page F-12 in general terms was applied to each of your agreements. In doing so, please address the following:
 - Disclose the deliverables, units of accounting, the arrangement consideration and how it was allocated including the method used to determine selling prices as discussed in 605-25-30-2 and provide all disclosures, as applicable, as required by ASC 605-25-50.
 - Disclose the accounting for the rights granted to Celgene to exercise options on a certain number of products.
 - Clarify your statements on page F-34 that your agreement with Merck and both your agreements with Lilly were not considered to be multiple element arrangements.
 - Revise your accounting policy disclosures to clarify your accounting for contract amendments and subsequent contracts entered into with the same party such as the December 2014 amended agreement with Merck and the October 2014 and April 2016 subsequent agreements with Lilly and GSK, respectively. In this regard, disclose your rationale for accounting for the amended/subsequent agreements as a new arrangement or as in-substance one arrangement.
 - Clarify with respect to the Lilly (December 2013), GSK (April 2016) and Daiichi agreements why it was appropriate to have recognized revenue over a period that your substantial performance obligations were met, when it appears you continue to have obligations as evidenced by the fact that you have the potential to earn future milestones.
 - You indicate that “Commercialization milestone payments may include payments triggered by annual product sales that achieve pre-specified thresholds.” Clarify whether this description relates to the “commercial” milestones listed in your separate disclosure herein for each agreement and whether or not and why or why not these types of milestones meet the definition of a milestone in ASC 605-28-20. If these milestones do not meet the definition of a milestone, disclose your accounting policy for them.
 - For each agreement, provide us the amount of each milestone and a description of what will trigger its payment. If commercial milestones do not meet the definition of a milestone in ASC 605-28-20, you do not need to include those milestones in what you provide us.

Item 8. Exhibits and Financial Statement Schedules

43. We refer to your statement on page 169 that you intend to enter into new employment agreements with your named executive officers prior to the offering's closing. Please file these new employment agreements as exhibits to the registration statement. Refer to Item 8 of the Form F-1 and Item 601(b)(10)(iii) of Regulation S-K.

You may contact Ibolya Ignat at 202-551-3636 or Jim B. Rosenberg, Senior Assistant Chief Accountant, at 202-551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Dorrie Yale at 202-551-8776 or Erin Jaskot, Special Counsel, at 202-551-3442 with any other questions.

Sincerely,

/s/ Erin K. Jaskot, *for*

Suzanne Hayes
Assistant Director
Office of Healthcare and Insurance

cc: Riccardo Leofanti
Skadden, Arps, Slate, Meagher & Flom LLP