[redacted]

From: [redacted]
Sent: 23 March 2018 15:48
To: response
Cc: [redacted]
Subject: Emerging and Innovative Companies CP - biotech company listing

Dear HKEX,

Thank you for taking the initiative in promulgating the new listing rules for biotech companies.

[redacted]

Based on my experience and knowledge about the biotech sector in the U.S. and Asia, I would like to provide some personal feedback/comments on the consultation paper.

1. Sophisticated investor requirement:
   a. Definition in consultation paper: An investor that the Exchange considers to be sophisticated by reference to factors such as net assets or assets under management, relevant investment experience, and the investor's knowledge and expertise in the relevant field
   b. In footnote 4 on page 8 of the consultation paper, the HKEx explains that "This factor is intended to demonstrate that a reasonable degree of market acceptance exists for the applicant's R&D and Biotech Product. The Exchange may not require compliance with this factor where the applicant is a spin-off from a parent company if the applicant is able to otherwise demonstrate to the Exchange's satisfaction that a reasonable degree of market acceptance exists for its R&D and Biotech Product (for example, in the form of collaboration with other established R&D companies)."

Comments:

(a) It would be unfair to grant this exception only to "spun-off" biotech companies. Whether a biotech company is a spin-off or not, collaboration and/or funding from other established R&D companies speaks to its market acceptance.

(b) Collaboration with other established R&D companies or biotech/pharmaceutical companies is a common practice by biotech companies. In most cases, established biotech/pharma companies are more sophisticated than financial investors and therefore collaboration and/or funding by established biotech/pharma companies is a strong proof of market acceptance and should be treated as equal as an investment from a sophisticated investor. Therefore, instead of putting this exception in a footnote in small print, I would suggest the HKEx to include collaboration with, out-licensing to and/or funding by established biotech or pharmaceutical companies, or research institutes, universities or hospitals, or foundations focused on related diseases or technologies, relating to the Core Product or with the Biotech Company as an alternative to the Sophisticated Investor category. In the US, in addition to other biotech/pharma companies, sometimes biotech companies also receive funding from research institutes,

universities and hospitals which believe the biotech product is promising and hence makes an investment. Like biotech/pharma companies, these research institutes, universities and hospitals are also very knowledgeable about the disease, R&D and potential market. Therefore, they should also be treated as "Sophisticated Investors."

(c) I would like to bring to the attention to the HKEx that in the US, in addition to sophisticated investors in the traditional sense (VC/PE funds) and biotech/pharma companies, there is a growing trend for foundations (particularly foundations focused on driving disease R&D or certain breakthrough technologies) to be investors in biotech companies. A classic example of such investment (and with success) is the CF Fouindation's investment in Vertex when the latter was still a small biotech company. https://www.cff.org/About-Us/About-the-Cystic-Fibrosis-Foundation/CF-Fofield undation-Venture-Philanthropy-Model/ These foundations have extensive knowledge in biotech and about R&D in the related disease or technology area (often more sophisticated than most financial investors about R&D in relevant disease and technology areas and potential market acceptance and size) of the biotech product being developed. Therefore, these disease focused foundations shall be treated as "Sophisticated Investors" by definition and by precedent.

2. Clinical trial requirement in Paragraph #75:
   Relevant language in proposed draft rules:
   (b) Biologics
   (i) In the case of a Core Product that is a new biologic product, the applicant must demonstrate that it has completed Phase I clinical trials and the relevant Competent Authority has no objection for it to commence Phase II (or later) clinical trials.
   (ii) In the case of a Core Product that is a biosimilar, the applicant must demonstrate that it has completed at least one clinical trial conducted on human subjects, and the relevant Competent Authority has no objection for it to commence Phase II (or later) clinical trials to demonstrate bio-equivalency.

   Comments:

   Please note that in the fields of gene therapy, orphan drugs, oncology and some other disease areas, clinical trials are not required to be conducted in Phase I, Phase II, and Phase III sequentially. Now it is a common practice for clinical trials in these fields to be conducted as combined phase I/II clinical trial. In fact, FDA has granted numerous approvals for combined or parallel Phase I/II clinical trials (www.clinicaltrials.gov input "phase I/II" and select "USA" as the country to run a search, you will see that in the US alone there are more than 1,700 Phase I/II clinical trials.

   Therefore, the proposed language which requires the Biotech Company to demonstrate that "it has completed Phase I clinical trials and the relevant Competent Authority has no objection for it to commence Phase II (or later) clinical trials" would create a problem when it is applied to biotech companies in gene therapy, rare disease, and oncology and some other disease fields because on the one hand if such companies have got no objection from FDA to start the phase I/II clinical trial, it would have met the "no objection to phase II" requirement in HKEx's draft language, but on the other hand it would fail to meet the "has completed Phase I clinical trial" requirement which was drafted without taking into account a common practice in biotech industry.

   As the traditional Phase I clinical trial is to test on safety which statistically 70% of all drug candidates passed Phase I clinical trials, the fact that a drug (or biologic) has already passed Phase I clinical trial by the time of listing application should not mean much to investors when investing in a biotech company. In fact, it may create mislead the unsophisticated public investors to think that phase I clinical trial is a big hurdle (which is not because majority (70%) of drug candidates pass Phase I and Phase I has nothing to do with efficacy) and passing it is a major achievement by the biotech company. Instead of requiring for completion of Phase I for all types of drugs/biologics and all disease indications, the HKEx should take into account of current practice in biotech sector and defer that to the FDA. If based on IND-enabling animal safety or other data, FDA has no objection to start a combined Phase I/II clinical trial, then

the biotech company shall be allowed to proceed to listing. This is in line with HKEx's spirit to allow for listing for biotech companies ready to start Phase II clinical trials.

Proposed change:

(b) Biologics

(i) In the case of a Core Product that is a new biologic product, the applicant must demonstrate that (i) it has completed Phase I clinical trials and the relevant Competent Authority has no objection for it to commence Phase II (or later) clinical trials, or (ii) based on relevant IND-enabling animal safety study and/or other data, the relevant Competent Authority has no objection for it to commence a combined Phase I/II (or later) clinical trials.

3. R&D operation and managing research and trials:

18A.04

(5) details of the Biotech Company's research and development experience, including:

(a) details of its operations in laboratory research and development;

(b) the collective expertise and experience of key management and technical staff; and

(c) its collaborative development and research agreements;

(11) if relevant and material to the Biotech Company's business operations, information on the following:—

(d) its historical experience of dealing with the concerns of local governments and communities on the sites of its research and trials, and relevant management arrangements;

Comments:

In today world, many biotech companies (and big pharmaceutical companies such as Pfizer and Merck) rely heavily on external contract research organization (CROs) and contract manufacturing organizations (CMOs) for its R&D operations and managing clinical trials, such as WuXi Apptech, Charles River, Covance, etc. That's why and how a small biotech company whose management cannot speak any foreign language or never been to a foreign country can have global R&D operations or conduct global multi-center clinical trials. Therefore, a biotech company may not need an internal laboratory for conducting research and development. To clarify on this point, suggest change 18A.04 (5)(a) to:

details of its operations in laboratory research and development and state whether such operations is through internal laboratory or external CROs and/or CMOs;

For managing research and clinical trials in different countries, many biotech companies (and even big pharma) rely on their local research collaborators and CROs. Hence, to clarity on this point, suggest change 18A.04(11)(d) to:

(i) its historical experience of dealing with the concerns of local governments and communities on the sites of its research and trials, and relevant management arrangements, or

(ii) if applicable, the experience of its research collaborator or the contract research organization (CRO) it engages in dealing with the concerns of local governments and communities on the sites of its research and trials, and relevant management arrangements, as applicable.

When HKEX responds to comments in public, please kindly keep my comments anonymous.
Thank you for your consideration.

Regards,

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