

IMPORTANT

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If you are in any doubt as to any aspect of this circular or as to the action to be taken, you should consult your stockbroker or other registered dealer in securities, bank manager, solicitor, professional accountant or other professional advisers.

If you have sold or transferred all your shares in Extrawell Pharmaceutical Holdings Limited, you should at once hand this circular and the accompanying form of proxy to the purchaser or the transferee or to the bank, stockbroker or other agent through whom the sale or transfer was effected for transmission to the purchaser or the transferee.



EXTRAWELL PHARMACEUTICAL HOLDINGS LIMITED

精優藥業控股有限公司*

(incorporated in Bermuda with limited liability)

(Stock Code: 00858)

CIRCULAR IN RESPECT OF THE RATIFICATION ACTIONS FOR THE ACQUISITION OF 51% INTEREST IN SMART ASCENT IN 2004

CONNECTED AND DISCLOSEABLE TRANSACTION AND NOTICE OF SPECIAL GENERAL MEETING

Independent financial adviser to the Independent Board Committee
and the Independent Shareholders



SOMERLEY LIMITED

A letter from the Board is set out on pages 5 to 21 of this circular. A letter from the Independent Board Committee is set out on page 22 of this circular. A letter from Somerley containing its advice to the Independent Board Committee and the Independent Shareholders is set out on pages 23 to 51 of this circular.

Notice of the SGM to be held at Harbour View Room III & IV, 3rd Floor, The Excelsior, Hong Kong, 281 Gloucester Road, Causeway Bay, Hong Kong on Monday, 8 June 2009 at 11:00 a.m. is set out on pages 131 to 132 of this circular. Whether or not you are able to attend the SGM, you are requested to complete the accompanying form of proxy in accordance with the instructions printed thereon and return the same to the Company's branch share registrar in Hong Kong, Tricor Tengis Limited at 26th Floor, Tesbury Centre, 28 Queen's Road East, Wanchai, Hong Kong as soon as possible and in any event not less than 48 hours before the time appointed for holding of the SGM or any adjournment thereof. Completion and return of the form of proxy shall not preclude you from attending and voting at the SGM or any adjournment thereof if you so wish.

* For identification purpose only

21 May 2009

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DEFINITIONS

In this circular, unless the context requires otherwise, the following expressions have the following meanings:

“2004 Acquisition”	the acquisition by Extrawell BVI of the Sale 51% Interest from the Vendors pursuant to the 2004 Agreement
“2007 Acquisition”	the acquisition by Extrawell BVI of the Sale 49% Interest from Mr. Ong pursuant to the 2007 Agreement, as more particularly referred to in the 2007 Circular and as supplemented by this circular
“2004 Agreement”	a conditional sale and purchase agreement dated 3 March 2004 entered into between the Vendors as vendors and Extrawell BVI as purchaser in connection with the sale and purchase of the Sale 51% Interest
“2007 Agreement”	a conditional agreement dated 27 July 2007 entered into between Mr. Ong as vendor and the Group as purchaser in connection with the sale and purchase of the Sale 49% Interest
“2004 Announcement”	the announcement dated 3 March 2004 issued by the Company in relation to the 2004 Acquisition
“2007 Announcement”	the announcement dated 1 August 2007 issued by the Company in relation to the 2007 Acquisition
“2004 Circular”	the circular issued by the Company on 25 March 2004 containing information on the 2004 Acquisition
“2007 Circular”	the circular issued by the Company on 22 August 2007 containing information on the 2007 Acquisition
“Associates”	have the same meanings ascribed thereto under the Listing Rules
“Board”	board of Directors
“Business Day”	a day (excluding Saturday and any day on which a tropical cyclone warning no. 8 or above or a “black” rainstorm warning is hoisted or remains hoisted between 9:00 a.m. and 12:00 noon and is not lowered at or before 12:00 noon) on which licensed banks in Hong Kong are open for business
“Company”	Extrawell Pharmaceutical Holdings Limited, a company incorporated in Bermuda with limited liability and whose Shares are listed on the main board of the Stock Exchange
“Consideration Shares”	the 300 million new Shares to be allotted and issued, credited as fully paid, to Mr. Ong as consideration under the 2007 Acquisition

DEFINITIONS

“Directors”	the directors of the Company
“Extrawell BVI”	Extrawell (BVI) Limited, a company incorporated in the British Virgin Islands with limited liability and a wholly-owned subsidiary of the Company
“Fosse Bio”	Fosse Bio-Engineering Development Limited, a company incorporated in Hong Kong with limited liability, 51% interests of which are owned by Smart Ascent
“Group”	the Company and its subsidiaries
“Hong Kong”	the Hong Kong Special Administrative Region of the PRC
“HK\$”	Hong Kong dollars, the lawful currency of Hong Kong
“Independent Board Committee”	the committee of the Board established for the purpose of advising the Independent Shareholders on the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby, the members of which include all the independent non-executive Directors, namely Mr. Fang Lin Hu, Mr. Xue Jing Lun and Ms. Jin Song
“Independent Shareholders”	Shareholders, other than the Vendors, Mr. Ho and their respective Associates and any connected persons who have material interests in the 2004 Acquisition and all other transactions contemplated under the 2004 Agreement
“Invention”	an invention “一種製備口服胰島素油相製劑的方法” (a method of production of oil-phase preparation of oral insulin), which is a patent registered under the joint name of Fosse Bio and Tsinghua University, Beijing under the registration numbers of ZL 01 1 15327.X (in respect of the PRC patent registration) and US 7,018,980 B2 (in respect of the United States patent registration)
“Latest Practicable Date”	18 May 2009, being the latest practicable date prior to the printing of this circular for ascertaining certain information contained herein
“Listing Rules”	Rules Governing the Listing of Securities on the Stock Exchange
“Medicine”	Oral Insulin Enteric-Coated Soft Capsules (口服胰島素腸溶膠丸), one of the oral insulin products developed by Fosse Bio in collaboration with Tsinghua University, Beijing
“Mr. Ho”	Mr. Ho Chin Hou, a former executive Director who had been a Director at the time of the 2004 Agreement, and who had resigned as Director with effect from 12 March 2009

DEFINITIONS

“Mr. Ong”	Mr. Ong Cheng Heang, one of the Vendors of the 2004 Acquisition and the vendor of the 2007 Acquisition, and the son-in-law of Mr. Ho
“Ms. Wu”	Ms. Wu Kiet Ming, one of the Vendors of the 2004 Acquisition, and the daughter-in-law of Mr. Ho
“Oral Insulin Products”	such oral insulin products as engaged by Fosse Bio to be developed by Tsinghua University, Beijing under the THU Collaboration Arrangement
“Outstanding Amount”	the Outstanding Purchase Price, together with all costs (including legal costs), expenses or other liabilities which any of Smart Ascent or Extrawell BVI may incur (if any) in connection with the payment of the Outstanding Purchase Price, which the Vendor and Ms. Wu Kiet Ming had jointly and severally undertaken and be responsible to pay in full such Outstanding Purchase Price for and on behalf of Smart Ascent if and when it becomes due and payable by Smart Ascent pursuant to the deed of transfer entered into by Smart Ascent for its acquisition of 51% interest in the share capital of Fosse Bio
“Outstanding Purchase Price”	an aggregate amount of HK\$31.78 million, being part of the consideration payable by Smart Ascent for its acquisition of 51% interests in the issued share capital of Fosse Bio in November 2003, which remained outstanding as at the Latest Practicable Date
“PRC”	the People’s Republic of China
“Relevant Technologies”	the technologies (including the right of patent) developed or to be developed by Tsinghua University, Beijing under the THU Collaboration Arrangement
“Sale Shares”	the aggregate of 5,100 ordinary shares of HK\$1.00 each in the issued share capital of Smart Ascent
“SFDA”	State Food and Drug Administration of the PRC
“SFO”	Securities and Futures Ordinance, Cap 571 of the Laws of Hong Kong
“SGM”	the special general meeting of the Company to be held at Harbour View Room III & IV, 3rd Floor, The Excelsior, Hong Kong, 281 Gloucester Road, Causeway Bay, Hong Kong on Monday, 8 June 2009 at 11:00 a.m. for the purpose of approving the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby

DEFINITIONS

“Share(s)”	ordinary share(s) of HK\$0.01 each in the share capital of the Company
“Shareholder(s)”	holder(s) of Share(s)
“Smart Ascent”	Smart Ascent Limited, a company incorporated in Hong Kong with limited liability, the entire issued share capital of which is owned as to 51% by Extrawell BVI and 49% by Mr. Ong
“Smart Ascent Group”	Smart Ascent and its subsidiaries
“Somerley”	Somerley Limited, a corporation licensed to carry out business in type 1 (dealing in securities), type 4 (advising on securities), type 6 (advising on corporate finance) and type 9 (asset management) regulated activities under the SFO and is the independent financial adviser to the Independent Board Committee and the Independent Shareholders in connection with the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby
“Stock Exchange”	The Stock Exchange of Hong Kong Limited
“THU Collaboration Arrangement”	the agreements dated 14 October 1998, 9 November 1998 and 15 October 1998 entered into between, among others, Fosse Bio and Tsinghua University, Beijing, the PRC regarding, among other matters, research and development of the use of Oral Insulin Products
“Vendors”	collectively, Ms. Wu and Mr. Ong
“Welly Surplus”	Welly Surplus Development Limited, a company incorporated in Hong Kong with limited liability and is owned as to 51% by Smart Ascent
“%”	per cent.

LETTER FROM THE BOARD



EXTRAWEILL PHARMACEUTICAL HOLDINGS LIMITED

精優藥業控股有限公司*

(incorporated in Bermuda with limited liability)

(Stock Code: 00858)

Executive Directors:

Dr. Mao Yu Min
Dr. Xie Yi
Dr. Lou Yi
Ms. Wong Sau Kuen

Registered office:

Clarendon House
2 Church Street
Hamilton HM11
Bermuda

Independent non-executive Directors:

Mr. Fang Lin Hu
Mr. Xue Jing Lun
Ms. Jin Song

*Head office and principal place
of business in Hong Kong:*

Room 3409–10, 34/F
China Resources Building
26 Harbour Road
Wanchai, Hong Kong

21 May 2009

To the Shareholders

Dear Sir or Madam

**CIRCULAR IN RESPECT OF THE RATIFICATION ACTIONS FOR
THE ACQUISITION OF 51% INTEREST IN SMART ASCENT IN 2004**

**CONNECTED AND DISCLOSEABLE TRANSACTION
AND
NOTICE OF SPECIAL GENERAL MEETING**

1. BACKGROUND

Reference is made to the 2004 Announcement and the 2004 Circular issued by the Company on the 2004 Acquisition. Under the 2004 Acquisition, the Group entered into the 2004 Agreement with the Vendors whereby the Group agreed to acquire and the Vendors agreed to sell 51% of the entire issued share capital of Smart Ascent. The 2004 Acquisition was completed on 17 August 2004.

It was stated in the 2004 Announcement and the 2004 Circular that the 2004 Acquisition constituted a discloseable transaction of the Company pursuant to the Listing Rules and, apart from Mr. Ong being an independent non-executive Director prior to his resignation from the office on 2 August 2001, each of the Vendors and their respective associates was independent from and not connected with

* For identification purpose only

LETTER FROM THE BOARD

any of the Directors, chief executives or substantial shareholders of the Company or any of its subsidiaries or any of their respective associates. As disclosed in the Company's clarification announcement dated 17 September 2007, it came to the attention of the Board that Mr. Ong is the son-in-law of Mr. Ho and Ms. Wu is the daughter-in-law of Mr. Ho. Under Rule 14A.11 of the Listing Rules, the definition of "connected person" includes a son-in-law and a daughter-in-law of a Director whose association with the Director is such that, in the opinion of the Stock Exchange, the transaction should have been subject to the connected transaction requirements under the Listing Rules. In its letter of 20 September 2007 to the Company, the Stock Exchange indicated its views that, taking into account the association of Mr. Ho with the Vendors as aforesaid, the 2004 Acquisition should have been subject to the relevant reporting, announcement and Independent Shareholders' approval requirements under Chapter 14A of the Listing Rules. At the request of the Stock Exchange, the SGM will be convened to seek the ratification and approval of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby by the Independent Shareholders.

Reference is also made to the 2007 Announcement and the 2007 Circular on the 2007 Acquisition. Under the 2007 Acquisition, the Group entered into the 2007 Agreement whereby Mr. Ong has conditionally agreed to sell and the Group has agreed to acquire the remaining 49% interests in Smart Ascent.

The purpose of this circular is to provide you with information in relation to the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby, the advice of the Independent Board Committee and the letter of advice from Somerley to the Independent Board Committee and the Independent Shareholders.

2. THE 2004 AGREEMENT DATED 3 MARCH 2004

Parties

Purchaser: Extrawell BVI, a wholly-owned subsidiary of the Company.

Vendors: Mr. Ong and Ms. Wu.

Mr. Ong was an independent non-executive Director prior to his resignation on 2 August 2001. He is also the son-in-law of Mr. Ho, a former executive Director who had been a Director at the time of the 2004 Agreement, and who had resigned as Director with effect from 12 March 2009. Ms. Wu is the daughter-in-law of Mr. Ho.

Assets acquired under the 2004 Acquisition

5,100 shares of HK\$1 each in the share capital of Smart Ascent, as to 5,000 shares by Ms. Wu and 100 shares by Mr. Ong, representing in aggregate 51% of the issued share capital of Smart Ascent.

LETTER FROM THE BOARD

Principal terms of the 2004 Agreement

(a) *Consideration*

Under the 2004 Agreement, the consideration (“**2004 Acquisition Consideration**”) payable by the Company to the Vendors for the 2004 Acquisition was HK\$73 million, as to HK\$71,568,628 to Ms. Wu and HK\$1,431,372 to Mr. Ong. The 2004 Acquisition was further adjusted to HK\$72,817,130, as to HK\$71,389,344 to Ms. Wu and HK\$1,427,786 to Mr. Ong, due to the adjustment thereto in the manner as set out in the paragraph (c) below and, after making such adjustment, the 2004 Acquisition Consideration was and had been paid in the following manner:

- (i) on or prior to the signing of the 2004 Agreement on 3 March 2004, a sum of HK\$20 million had been paid by or on behalf of Extrawell BVI to the Vendors in the following manner, which had been applied to satisfy payment of a pro tanto amount of the 2004 Acquisition Consideration upon completion of the 2004 Acquisition:
 - (aa) an aggregate of HK\$5 million has been paid by Extrawell BVI to Ms. Wu (as receiving agent for the Vendors) in cash on or prior to the date of the 2004 Agreement as the earnest money pursuant to the memorandum of understanding entered into between Extrawell BVI and the Vendors on 7 January 2004; and
 - (bb) Extrawell BVI paid a sum of HK\$15 million as the balance of the Deposit upon signing of the 2004 Agreement;
- (ii) on or before completion of the 2004 Acquisition on 17 August 2004, an aggregate sum of HK\$16.5 million, being the balance of half of the 2004 Acquisition Consideration, had been paid by Extrawell BVI to the Vendors in cash; and
- (iii) upon evidence being supplied to Extrawell BVI to Extrawell BVI’s reasonable satisfaction that Fosse Bio has entered into agreement(s) with hospitals and/or medical institutions to carry out the Phase II of the clinical trial of the Medicine, Extrawell BVI should within 10 Business Days from the date of Extrawell BVI’s receipt of the said evidence pay or procure payment to the Vendors an aggregate sum of HK\$36,317,130 being the remaining balance of the 2004 Acquisition Consideration as adjusted in the manner as set out in paragraph (c) below, as to HK\$35,605,030 paid to Ms. Wu or her nominee and as to HK\$712,100 to Mr. Ong or his nominee. Such balance was settled by the Group during the year ended 31 March 2005.

The 2004 Acquisition Consideration had been financed by the Group out of its own internal resources.

The 2004 Acquisition Consideration had been determined between the Group and the Vendors after arm’s length negotiations with reference to the then valuation of Fosse Bio as at 31 January 2004 of about HK\$279.8 million as appraised by Castores Magi Asia Limited, an independent professional valuer.

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Your attention is also drawn to the latest valuation report dated 21 May 2009 prepared by Castores Magi Asia Limited as set out in appendix I to this circular in respect of the market value of the Smart Ascent Group as at 28 February 2009. Based on the valuation report, the appraised market value of Smart Ascent Group as at 28 February 2009 amounted to HK\$1,547,241,000. Castores Magi Asia Limited has used discounted cash flow method in evaluating the Smart Ascent Group.

(b) *Conditions precedent and completion of the 2004 Acquisition*

Completion of the 2004 Acquisition had been conditional upon, among other conditions, the following conditions:

- (i) a legal opinion to be issued by PRC lawyers acceptable to Extrawell BVI, which should cover (but not limited to) the legality and validity of the THU Collaboration Arrangement, in such form and substance to the satisfaction of Extrawell BVI having been obtained;
- (ii) none of the warranties as set out in the 2004 Agreement having been breached in any material respect (or, if capable of being remedied, has not been remedied) or misleading or untrue in any material respect;
- (iii) if required, all approvals, consents, authorizations and licenses in relation to the transactions contemplated under the 2004 Agreement having been obtained from the relevant governmental authorities or other third parties;
- (iv) evidence being supplied to Extrawell BVI to Extrawell BVI's reasonable satisfaction that Fosse Bio has completed the report for the completion of phase I of the clinical trial of the Medicine as referred to in the SFDA's approval for clinical trial of medicine no. 2003L02797 (國家食品藥品監督管理局藥物臨床批件批件號 2003L02797) and is entitled to proceed with the phase II of the clinical trial of the same; and
- (v) if required, the approval by the independent Shareholders of the 2004 Agreement and the transactions contemplated thereby and all other consents and acts required under the Listing Rules being obtained and completed or, as the case may be, the relevant waiver from compliance with any of such rules being obtained from the Stock Exchange.

Completion of the 2004 Acquisition took place on 17 August 2004.

(c) *Treatment of the outstanding amount due to the Vendors*

Prior to the signing of the 2004 Agreement, Smart Ascent had owed to the Vendors in an aggregate sum of approximately HK\$12.7 million representing the Vendors' advances made to and expenses incurred for Smart Ascent and Fosse Bio for the purpose of their operations and for financing the research and development and related activities in connection with the THU Collaboration Arrangement, and such sum remained outstanding at the time of the 2004 Agreement. Under the 2004 Agreement, the Vendors and Extrawell BVI had agreed that such amount would continue to be repayable by Smart Ascent to the Vendors but, had the net asset value of Smart Ascent been less than zero as at the completion of the 2004 Acquisition, the

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Vendors had agreed and undertaken to pay to Extrawell BVI an amount equals to that which would make Smart Ascent's unconsolidated net asset value to become zero, and the 2004 Acquisition Consideration would be adjusted accordingly. In such event and without prejudice to Extrawell BVI's right to seek recourse against the Vendors, Extrawell BVI was entitled to set off the amount to be adjusted against such outstanding advances from the Vendors. Accordingly, the 2004 Acquisition Consideration had been adjusted from HK\$73 million to HK\$72,817,130. As at the Latest Practicable Date, there was no amount due from Smart Ascent to the Vendors.

(d) Treatment of the outstanding amount owed by Smart Ascent

Smart Ascent acquired its 51% interests in the issued share capital of Fosse Bio from one of its existing shareholders, Fordnew Industrial Limited ("**Fordnew**") at a consideration of HK\$39.78 million in November 2003 and, pursuant to a deed of transfer entered into between Fordnew and Smart Ascent in February 2004, such consideration would be payable by Smart Ascent to Fordnew in four instalments, the first two instalments for an aggregate sum of HK\$8 million had been paid by Smart Ascent prior to the date of the 2004 Agreement, whereas the balance of the consideration for the sum of HK\$31.78 million, being the Outstanding Purchase Price, shall be payable by Smart Ascent to Fordnew in the following manner:

- (i) as to HK\$12 million, within 14 days from the service of Fordnew's notice of the issuance of certificate of phase III clinical trial of the Medicine issued by the SFDA and the production of the original certificate for inspection by Smart Ascent; and
- (ii) as to the balance of HK\$19.78 million, within 14 days from the service of Fordnew's notice of the issuance of certificate of new medicine (新藥證書) for the Medicine issued by the SFDA and the production of the original certificate for inspection by Smart Ascent.

Under the 2004 Agreement, the Vendors had jointly and severally undertaken to the Group that they will be responsible to pay in full the Outstanding Amount (being the Outstanding Purchase Price and all costs (including legal costs), expenses or other liabilities which any of Smart Ascent or Extrawell BVI may incur (if any) in connection with the payment of the Outstanding Purchase Price) for and on behalf of Smart Ascent if and when it becomes due and payable by Smart Ascent pursuant to the said deed of transfer. As security for the Vendors' payment obligations in respect thereof, Mr. Ong had, since the completion of the 2004 Acquisition, pledged his 49% interests in the issued share capital of Smart Ascent to Extrawell BVI.

(e) Application for patent registration

The Vendors had unconditionally and irrevocably undertaken to Extrawell BVI that the Vendors together with Extrawell BVI will use all reasonable endeavours to procure Fosse Bio to apply for and/or complete the registration of patent in respect of the Medicine (including the Invention). The patent registration in respect of the Invention had been completed under the registration numbers of ZL 01 1 15327.X (in respect of the PRC patent registration) and US 7,018,980 B2 (in respect of the United States patent registration).

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(f) *Other warranties and undertakings*

Under the 2004 Agreement, the Vendors had also given comprehensive warranties, representations and undertakings to Extrawell BVI in relation to, among other matters, the state of affairs of Smart Ascent, Fosse Bio, the THU Collaboration Arrangement, the intellectual property rights in respect of the Relevant Technologies and/or the Medicine, the more important of which included:

- (i) all intellectual property rights appertaining to the Relevant Technologies developed or to be developed as specified in the THU Collaboration Arrangement, including the right of patent, should belong to Fosse Bio and Tsinghua University, Beijing jointly, and Fosse Bio should be entitled to commercialise such of the Relevant Technologies as specified therein and to manufacture in the PRC and sell the Oral Insulin Products derived therefrom in accordance with the provisions of the THU Collaboration Arrangement on an exclusive basis;
- (ii) Fosse Bio had fully performed its obligations under the THU Collaboration Arrangement, including but not limited to its obligations to make payment thereunder or in connection therewith and to make application for the clinical trials of the Oral Insulin Products in conjunction with Tsinghua University, Beijing;
- (iii) Fosse Bio had obtained the requisite approvals from the competent authorities in the PRC (being SFDA) for conducting phases I and II of the clinical trials of the Medicine, and there had been no fact or matter known to either or both of the Vendors or which would or is likely to give rise to any revocation, cancellation or alternation of the terms and conditions of the said approvals;
- (iv) neither of Smart Ascent and Fosse Bio had received any notice or was otherwise aware of any infringement of or conflict with asserted rights of others with respect to any rights in respect of the Medicine, or of any facts which would render any such rights invalid or inadequate to protect the interests of Smart Ascent (or, as the case may be, Fosse Bio) and which were materially adverse to its business;
- (v) neither of Smart Ascent and Fosse Bio had (otherwise than in the ordinary and normal course of business and to its staff and officers whose province it is to know and its professional advisers) disclosed, or permitted to be disclosed, or undertaken or arranged to disclose, to any person other than Extrawell BVI any of its know-how, trade secrets, confidential information, price lists or lists of customers or suppliers;
- (vi) all information stated in the reports in respect of the results of the clinical trials of the Medicine, which were prepared by the hospitals designated by SFDA for conducting clinical trials for phases I and II of the clinical trials of the Medicine, as provided to Extrawell BVI, the auditors of the Company, the valuer of the Company or other authorised agents of Extrawell BVI had been accurate and comprehensive in all material respects;

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- (vii) within 12 months from the date of completion of the 2004 Acquisition and for so long as such Vendor remains as a director and/or shareholder of Smart Ascent and/or Fosse Bio, whichever is the later, he/she will not, either alone or jointly with or as manager or agent for any person, firm or company directly or indirectly and whether or not for gain, be engaged or interested in or concerned with any business which is in any respect in competition with or similar to any business of Smart Ascent and/or Fosse Bio; and
- (viii) the Vendors will not at any time use either on his/her own account or for others or partly for himself/herself and partly for others the trade secrets or other confidential information of Smart Ascent and/or Fosse Bio (including but not limited to knowledge of and know-how relating to or in connection with Smart Ascent and/or Fosse Bio, any of their business and/or the Relevant Technologies and/or the Medicine).

Reasons for and benefits of the 2004 Acquisition

Prior to the entering into of the 2004 Acquisition, the Group had been principally engaged in the marketing and distribution of pharmaceutical products, health care and nutritional products, and medical appliances and equipment to customers in the PRC, and the development, manufacture and distribution of pharmaceutical products in the PRC. The 2004 Acquisition had been regarded as an investment opportunity for the Group to diversify its product base and to thereby enhance its profitability. As Fosse Bio will be entitled to commercialise the Relevant Technologies and to manufacture and sell the Oral Insulin Products, in particular the Medicine, on an exclusive basis once the necessary clinical trials have been completed and the requisite new medicine certificate in respect of the Medicine has been obtained, and as oral insulin will be a new method for treatment of diabetes, the Directors are of the view that the 2004 Acquisition enabled the Group to capture the business opportunities arising from the launch of the oral insulin in the worldwide market in the future. Accordingly, the Directors, including the independent non-executive Directors having taken into account the advice of Somerley, consider that the 2004 Acquisition to be in the interest of the Company and its shareholders as a whole despite the past loss-making performance of Smart Ascent and/or Fosse Bio.

The Directors, including the independent non-executive Directors having taken into account the advice of Somerley, consider that the terms of the 2004 Agreement are fair and reasonable and in the interest of the Company and its shareholders as a whole.

Risks in connection with the 2004 Acquisition

Set out below are some risks which the Board considers relevant to the 2004 Acquisition.

Final approval for production and distribution of Medicine not yet obtained

As discussed in the section headed “Information on Smart Ascent” below, on 30 April 2008, the SFDA granted approval to Fosse Bio and Tsinghua University, Beijing to undertake further clinical trial of the Medicine. In the said approval, the SFDA had imposed more stringent requirements in respect of the next phase clinical trial compared to the phase II clinical trial. As at the Latest Practicable Date, the Group was liaising with hospitals and conducting other preparatory work for the clinical trial. The Company expects the clinical trial to commence in late June 2009.

LETTER FROM THE BOARD

From the Group's experience, it is expected that the further clinical trial will be completed and the report thereof will be prepared for approval by the SFDA by March 2010. However, such further clinical trial is subject to evaluation and queries by SFDA and it is possible that the SFDA may not approve the manufacturing and distribution of the Medicine.

There is a risk that Fosse Bio may not be able to obtain all licences, certificates and permits from the relevant regulatory authorities in the PRC required for formal production and distribution of the Medicine.

Should Fosse Bio fail to obtain the necessary approvals from the relevant authorities, it may not be able to commence the production and distribution of the Medicine in the PRC, which could have material and adverse impact on the business and financial results of Fosse Bio, and in turn the Group's business and financial results. The Group may also have to write-off or suffer impairment on the carrying values of the technological know-how in relation to the Relevant Technologies, which amounted to approximately HK\$284.3 million as at 31 March 2008.

Funding requirement

The Company estimates that Fosse Bio will further incur approximately HK\$16 million of research and development expenses in relation to the next phase clinical trial, and an addition amount of approximately HK\$6 million for pre-marketing efforts before the commencement of commercial production and distribution of the Medicine. Should the actual development and pre-marketing expenses turn out to be much higher than the above amounts and that the Group is unable to inject sufficient funding to support further development of the Medicine due to working capital needs from its existing operations, the oral insulin project may not be able to complete and commercialise successfully.

Manufacturing and distribution

As at the Latest Practicable Date, the manufacturing plant for the Medicine was still under construction. Other than a small scale production of the Medicine for clinical trials, the Group has not yet commenced production of the Medicine. Should the manufacturing techniques prove to be faulty or a major processing reengineering has to be performed before mass scale production, a significant delay to the timing of the launch of the Medicine would be likely.

The Group expects to appoint two distributors in each of 30 major cities in the PRC for distribution of the Medicine during the initial stage. In case such appointment of distributors cannot be completed on time, or disagreement on terms of appointment arise, or the sales channels prove to be too weak to promote sales of the Medicine, the target market share of the Medicine may not be reached.

Market acceptance and competition

It is assumed in the financial projections of Smart Ascent that Fosse Bio would gain an increasing market share during the forecast period from October 2010 to March 2015. However, there can be no assurance that the Medicine can gain sufficient market acceptances in the PRC diabetic market to achieve the projected revenue. The level of market penetration, sales and pricing

LETTER FROM THE BOARD

can only be broad estimates at this stage. In case it cannot be demonstrated in the next phase clinical trial that the Medicine has any sustained improvement over existing treatments, Fosse Bio may not be able to gain sufficient market acceptances to support the estimated revenue.

In assessing the acceptance of the new Medicine to be launched to the market, diabetic patients may compare the pricing of the Medicine with other medical products. If the pricing assumption made by the Group proves too optimistic, target diabetics may continue to use their existing drugs instead of the Medicine.

The effectiveness of the Medicine may be over-estimated and its side-effects may emerge when the Medicine is widely used. There are precedent cases of seemingly promising new drugs which failed to become established. Exubera, an inhalable insulin introduced by Pfizer Incorporated which was available in the United States from 2006 to 2007 and considered a new method of insulin intake, was withdrawn from the market after it failed to gain acceptances among diabetic patients.

If the Medicine is approved and introduced to the market successfully, there appears to be a large potential market of diabetes patients in the PRC. Nevertheless, rival products could emerge and, as noted above, the sales price is yet to be tested in the market. Competition from existing insulin products in the PRC market may also create uncertainty as to the projected revenue of Fosse Bio. Although the Company considered that the Medicine is likely to be the first oral insulin to be distributed in the PRC upon successful commercialisation, potential customers might still consider different factors when choosing among different diabetic drugs available in the market, which include pricing, branding and reputation, availability, convenience of use and certain other factors. Besides, the possibility of oral insulin with similar technologies or insulin with other delivery methods being developed, or existing oral anti-diabetic drugs (“OADs”) available in the PRC market being sold more aggressively by competitors, may also impact the financial results of Fosse Bio.

Expiry of patent of the Relevant Technologies

The patent issued by the PRC authorities for the Relevant Technologies will expire in April 2021, after which the Medicine could become “generic”, and there is no assurance that other market competitors may manufacture and sell the Medicine on their own. Intensifying competition in the market may have negative impact on the pricing and the profit margin of the Medicine and may thereby have adverse effect on the profitability of the Group.

Product concentration

The financial projections of the oral insulin project prepared by the Company are based solely on the sales of the Medicine, which account for 100% of the revenue to be generated by Fosse Bio. In the event that the Medicine is not successfully commercialised in the PRC market, or the sales price/sales volumes of the Medicine do not reach the projected amounts, the Smart Ascent Group’s total sales would be materially and adversely affected.

LETTER FROM THE BOARD

Fluctuations in cost of sales

According to the financial projections, the cost of the main component (insulin powder) and other components of the Medicine, account for a majority of the total cost of sales. The price of insulin powder and other cost components are subject to a number of factors such as supply and demand and the economic environment in the PRC at the time. The gross margin of Fosse Bio may be adversely affected if the purchase price of insulin powder or other components rise significantly.

Product liability

Fosse Bio could face material claims arising from any alleged harmful effect of the Medicine. There is no assurance that any product liability claim brought against the Group in respect of the Medicine would not have an adverse effect on Fosse Bio's business operations and financial results and position, and accordingly the Group's business operations and financial results and position.

Further information on certain risks in connection with the 2004 Acquisition are set out in the section headed "Risk Factors" in the letter of advice from Somerley to the Independent Board Committee and the Independent Shareholders in respect of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby set out on page 23 to page 51 of this circular.

Financial impact of the 2004 Acquisition

Upon completion of the 2004 Acquisition in August 2004, Smart Ascent became a 51%-owned subsidiary of Extrawell BVI, which is in turn wholly-owned by the Company. Smart Ascent had been accounted for as subsidiary of the Company and its financial results (including earnings, assets and liabilities) had been consolidated into and reflected in the financial statements of the Group since then.

The 2004 Acquisition had the following financial impacts on the Group in respect of its assets and results for each of the three years ended 31 March 2008 as follows:

(a) Earnings

For each of the financial years ended 31 March 2006, 2007 and 2008, the Group's turnover were approximately HK\$178.3 million, HK\$158.8 million and HK\$165.1 million respectively. As the SFDA's final approval required for launching of the Medicine has not been obtained, the Smart Ascent Group had not contributed any turnover during the financial periods concerned.

The Group's consolidated net profit/(loss) for each of the financial years ended 31 March 2006, 2007 and 2008 were approximately HK\$4.2 million, HK\$8.9 million, and (HK\$13.3 million) respectively; of which approximately HK\$4.7 million, HK\$9.3 million and (HK\$11.7 million) were attributable to the equity holders of the Company.

LETTER FROM THE BOARD

The net loss of the Smart Ascent Group included in the Group's results for each of the financial years ended 31 March 2006, 2007 and 2008 were HK\$278,381, HK\$215,481, and HK\$502,322 respectively; of which HK\$136,158, HK\$100,828 and HK\$242,404 were attributable to the equity holders of the Company.

Despite that no turnover has been generated from the Smart Ascent Group and its loss-making history principally attributable to the costs and expenses for the development of the Medicine since the completion of the 2004 Acquisition, the Directors are optimistic that the Smart Ascent Group can become one of the principal contributors to the Group's turnover and profit in the future after the successful launch of the Medicine in the market.

Nevertheless, should the Smart Ascent Group fail to obtain the certificate of new medicine in respect of the Medicine by the relevant PRC authority, there can be significant impact on the results of the Group, as it is expected that such failure can result in the following adjustments to the assets and liabilities of the Group and will, in turn, result in the net impairment loss for such amount representing the then carrying amount for the intangible assets represented by the technological know-how in relation to the production and the exclusive right for the commercialisation of the Medicine:

- (i) an impairment provision for the intangible assets represented by the technological know-how in relation to the production and the exclusive right for the commercialisation of the Medicine, the carrying value of which amounted to approximately HK\$284,260,000 as at 31 March 2008 of which HK\$93,986,460 will be attributable to the equity holders of the Company;
- (ii) a write off of the Smart Ascent Group's other receivables representing the amount of the Outstanding Purchase Price assumed by the Vendors under the 2004 Acquisition, which amounted to HK\$31,780,000 as at 31 March 2008; and
- (iii) a write off of the Smart Ascent Group's other payables representing the amount of the Outstanding Purchase Price payable by Smart Ascent, which amounted to HK\$31,780,000 as at 31 March 2008.

(b) *Assets and liabilities*

As at 31 March 2006, 2007 and 2008, the audited total assets of the Group were approximately HK\$571.3 million, HK\$610.0 million and HK\$619.6 million respectively, of which HK\$314.1 million, HK\$315.0 million and HK\$315.0 million were attributable to the Smart Ascent Group, representing 55.0%, 51.6% and 50.8% of the Group's total assets as at the said dates, respectively.

As at 31 March 2006, 2007 and 2008, the audited total liabilities of the Group were approximately HK\$70.6 million, HK\$93.5 million and HK\$106.7 million respectively, of which HK\$35.5 million, HK\$36.6 million and HK\$37.1 million were attributable to the Smart Ascent Group, representing 50.3%, 39.1% and 34.7% of the Group's total liabilities as at the said dates, respectively.

LETTER FROM THE BOARD

Should the Smart Ascent Group fail to obtain the certificate of new medicine in respect of the Medicine by the relevant PRC authority, there can be significant impact on the results of the Group, as it is expected that net assets value of the Group will be reduced by approximately HK\$284.3 million, of which HK\$93,986,460 is attributable to the equity holders of the Company upon making the adjustments as set out in paragraph (a) above. These represent 55.4% of the Group's net assets value as at 31 March 2008.

Save as disclosed above, the Directors do not expect any material impact on its assets and liabilities.

(c) *Cash flow*

The Company estimates that Fosse Bio will further incur approximately HK\$16 million of research and development expenses in relation to the next phase clinical trial, and an addition amount of approximately HK\$6 million for pre-marketing efforts before the commencement of commercial production and distribution of the Medicine. According to the shareholders' agreement of Fosse Bio, upon the request of Fordnew, Smart Ascent shall provide interest-free loan to Fosse Bio in proportion to its shareholding in Fosse Bio and/or provide interest-free loan to the other shareholders of Fosse Bio for onward lending to Fosse Bio for expenses relating to clinical trial. Given that the bank and cash balance of the Group amounted to approximately HK\$101 million (including pledged deposits of approximately HK\$20 million to secure banking facilities) as at the Latest Practicable Date, the Board agrees with the view of Somerley that the additional expenditure required for the oral insulin project can be funded by the Group from its internal resources.

3. INFORMATION ON SMART ASCENT

Smart Ascent is a private company incorporated in Hong Kong with limited liability, having an authorised share capital of HK\$10,000 divided into 10,000 shares of HK\$1 each, all of which have been issued and are fully paid and beneficially owned as to 51% by Extrawell BVI and 49% by the Vendor as at the Latest Practicable Date. Before the completion of the 2004 Acquisition in August 2004, Smart Ascent was owned as to 50% by Mr. Ong and 50% by Ms. Wu. According to the register of members of Smart Ascent, Smart Ascent was incorporated as a shelf company by corporate secretarial services agent in Hong Kong in December 2000 and was activated by two of the Group's former employees and the Group's then employees, Ms. Tang Po Ling and Ms. Chuah Meng Meng who purchased Smart Ascent from the corporate secretarial services agent in January 2001, and the two subscriber shares, being the then entire issued share capital of Smart Ascent, were initially transferred to and registered under the names of Ms. Tang and Ms. Chuah. As explained by the Vendors, since they were not residing in Hong Kong and had limited experience in the incorporation of Hong Kong company, they asked Mr. Ho for assistance who in turn arranged Ms. Tang and Ms. Chuah to purchase and activate Smart Ascent on their behalf for use as the investment vehicle for the project. According to the register of members of Smart Ascent, these shares were subsequently transferred back to the Vendors in March 2002 at nominal consideration, and the Vendors had become the only registered shareholders of Smart Ascent since then until the completion of the 2004 Acquisition. To the best of the Directors' knowledge, information and belief having made all reasonable enquiry, Ms. Tang and Ms. Chuah do not have, and did not have at the material time, any relationship with the Company and its connected persons other than as former

LETTER FROM THE BOARD

employees of the Group. Upon completion of the 2004 Acquisition in August 2004, Smart Ascent became an indirect non wholly-owned subsidiary of the Company and its financial results had been consolidated into the financial statements of the Group since then.

The aggregate original purchase cost of the Vendors of the 51% of the issued share capital of Smart Ascent was approximately HK\$6.6 million, being 51% of their aggregate amount of investment made by them to Smart Ascent since its incorporation and up to the completion of 2004 Acquisition, comprising approximately HK\$4.4 million expenses incurred for financing the research and development and related activities in connection with the THU Collaboration Arrangement, HK\$8 million for payment of the first two instalments of the consideration payable by Smart Ascent to Fordnew for the acquisition of 51% interest in Fosse Bio (as referred to in the paragraph “The 2004 Agreement dated 3 March 2004 — principal terms of the 2004 Agreement — Treatment of the outstanding amount owed by Smart Ascent” above), approximately HK\$10,000 for their payment of the share capital of Smart Ascent, approximately HK\$469,000 for general and other professional expenses incurred by or for Smart Ascent and approximately HK\$187,000 for their legal expenses incurred in respect of the 2004 Acquisition. In addition, the Vendors had undertaken to pay in full the Outstanding Amount.

Smart Ascent is an investment holding company. According to the register of members of Fosse Bio, Smart Ascent acquired from and became the holder of 51% interest in the issued share capital of Fosse Bio in November 2003, and the Directors are not aware of any written agreement or arrangement entered into between Smart Ascent and Fordnew in respect of such acquisition before then. Fosse Bio is principally engaged in the research and development of the Relevant Technologies pursuant to the THU Collaboration Arrangement. Since February 2006, it has also become the holding company of Welly Surplus, which is owned as to 51% by Smart Ascent. As disclosed in the Company’s announcement dated 24 October 2006, Welly Surplus has also entered into acquisition and cooperation agreements with an independent third party for the acquisition and construction of a new manufacturing plant in the PRC for the manufacturing of the Medicine, and will act as the manufacturing arm of the Group for the Medicine. As disclosed in the Company’s announcement dated 8 April 2009, under the relevant acquisition agreement, in the event that certain of the conditions to the agreement have not been fulfilled on or before 12:00 noon on 30 November 2007 (“**2006 Acquisition Long Stop Date**”) or such later date and time as the parties may mutually agree, the agreement shall forthwith terminate (save in respect of the confidentiality provisions thereof). As the time for completing the acquisition of the manufacturing plant is also dependent on the progress of construction of the plant, completion of the acquisition has not been taken place yet. In light of the expected progress of the application for registration of the Medicine, the parties have agreed to extend the 2006 Acquisition Long Stop Date to 30 June 2010 and that the independent third party shall procure the completion of the construction of the manufacturing plant on or before 30 June 2010 or, if the SFDA issues an approval (with or without conditions) to apply for the New Medicine Certificate for the Medicine, within nine months of the date of the said approval, whichever is earlier. If it is stated by the SFDA that phase III clinical trial in respect of the Medicine is required, the parties shall discuss and revise the construction schedule of the manufacturing plant accordingly.

Fosse Bio has entered into the THU Collaboration Agreement with Tsinghua University, Beijing for the joint research and development of the Relevant Technologies, including but not limited to the use of the Oral Insulin Products. Under the THU Collaboration Arrangement, Fosse Bio will be entitled to commercialise such of the Relevant Technologies as specified therein and to manufacture and sell the products derived therefrom in accordance with the provisions of the THU Collaboration Arrangement on

LETTER FROM THE BOARD

an exclusive basis, and Tsinghua University, Beijing shall be entitled to a royalty representing 1.5% of the sales of such products starting from the commercial production thereof. Mutual consent of Fosse Bio and Tsinghua University, Beijing is required in respect of any sale or transfer of the manufacturing right of any of the products so developed to a third party, in such the sales proceeds thereof shall be shared by them in equal shares.

The Invention is one of the Relevant Technologies under the joint research and development by Fosse Bio and Tsinghua University, Beijing under the THU Collaboration Arrangement, and they are also the joint registered owners of the patent in respect of the Invention. The Medicine, being the product derived from the Invention, completed its phase II of the clinical trials and the clinical trial report had been submitted to SFDA for review and approval. On 30 April 2008, the SFDA granted approval to Fosse Bio and Tsinghua University, Beijing to undertake further clinical trial of the Medicine. For the purpose of the further clinical trial, the Group was still liaising with hospitals and conducting other preparatory work for the clinical trial as at the Latest Practicable Date. From the Group's experience, it is expected that the further clinical trial will be completed and the report thereof will be prepared for approval by the SFDA by March 2010. Under the Administrative Regulations for Registration of Medicine of the PRC (藥品註冊管理辦法) (“**Regulations**”), the Medicine can be launched to the market upon completion of the relevant clinical trials and the grant of approval by the relevant PRC authority.

Based on the audited consolidated accounts of Smart Ascent, the consolidated net asset value of Smart Ascent was approximately HK\$277,914,300 as at 31 March 2008.

Based on the audited consolidated accounts of Smart Ascent, for the year ended 31 March 2007, the consolidated net loss before and after taxation and extraordinary items of Smart Ascent amounted to approximately HK\$215,500 and HK\$215,500 respectively, while for the year ended 31 March 2008, the consolidated net loss before and after taxation and extraordinary items of Smart Ascent amounted to approximately HK\$502,300 and HK\$502,300 respectively.

As disclosed in the Company's announcements dated 31 October 2007 and 16 January 2008, Mr. Ho and Mr. Ho Yu Ling (“**Mr. YL Ho**”), two of the former executive Directors, had been charged with charges (“**Charges**”) in connection with certain alleged misrepresentations and concealment of Mr. Ho's relationship with the Vendors by deceit. The Directors also note that there were articles appearing newspapers regarding the Charges and other allegations against one or both of them regarding their involvements in the 2004 Acquisition, acquisitions of interests in Smart Ascent and/or Fosse Bio. As these Charges were still under the relevant legal proceedings as at the Latest Practicable Date and there is limited publicly accessible information in relation to the Charges, the Company is not in the position to comment on or clarify these allegations other than the information as disclosed in this circular. The purpose of this circular is to set out all material information relating to the Smart Ascent Group and the 2004 Acquisition to the best of the Directors' knowledge, information and belief having made all reasonable enquiries.

4. IMPLICATIONS UNDER THE LISTING RULES

As the applicable percentage ratios (as calculated in accordance with Rule 14.07 of the Listing Rules) for the 2004 Acquisition are more than 5% but less than 25%, the 2004 Acquisition constituted a discloseable transaction of the Company under Rule 14.06 of the Listing Rules. Besides, as Mr. Ong is the son-in-law of Mr. Ho and Ms. Wu is the daughter-in-law of Mr. Ho and, pursuant to Rule 14A.11 of

LETTER FROM THE BOARD

the Listing Rules, the Stock Exchange is of its views that, taking into account the association of Mr. Ho with the Vendors as aforesaid, the 2004 Acquisition should have been subject to the relevant reporting, announcement and Independent Shareholders' approval requirements under Chapter 14A of the Listing Rules. At the request of the Stock Exchange, the SGM will be convened to seek the ratification and approval of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby by the Independent Shareholders.

The Vendors and Mr. Ho (who resigned on 12 March 2009, being less than 12 months from the date of the SGM, and hence a connected person of the Company within the meaning of the Listing Rules), who are or considered to be materially interested in the 2004 Acquisition, and their respective associates are therefore required to abstain from voting on the resolution proposed to be passed at the SGM for ratifying and approving the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby. To the best knowledge of the Directors after making reasonable enquiries, as at the Latest Practicable Date, none of the Vendors, Mr. Ho and their respective associates held any Shares.

While Mr. YL Ho, one of the former executive Directors, had been charged with five charges in connection with certain alleged misrepresentations and concealment of Mr. Ho's relationship with the Vendors by deceit, there was no allegation under these charges, and the Directors are not aware of any other circumstances, that may indicate that Mr. YL Ho and/or any of his associates is materially interested in the 2004 Acquisition. Nevertheless, Mr. YL Ho has indicated to the Board that he and his associate will abstain from voting on the resolution proposed to be passed at the SGM for ratifying and approving the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby. To the best knowledge of the Directors after making reasonable enquiries, as at the Latest Practicable Date, Mr. YL Ho was interested in 52,000,000 Shares, representing approximately 2.27% of the entire issued share capital of the Company, through a company wholly owned by him named Well Success Limited.

5. SGM

The Company will convene the SGM at Harbour View Room III & IV, 3rd Floor, The Excelsior, Hong Kong, 281 Gloucester Road, Causeway Bay, Hong Kong on Monday, 8 June 2009 at 11:00 a.m. to consider and, if thought fit, ratify and approve the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby.

Pursuant to Rule 13.39(4) of the Listing Rules, the vote of the Independent Shareholders taken at the SGM to ratify and approve the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby, will be taken by poll, the results of which will be announced after the SGM.

A notice convening the SGM is set out on pages 131 to 132 of this circular. Whether or not you are able to attend the SGM, you are requested to complete the accompanying form of proxy in accordance with the instructions printed thereon and return the same to the Company's branch share registrar in Hong Kong, Tricor Tengis Limited at 26th Floor, Tesbury Centre, 28 Queen's Road East, Wanchai, Hong Kong as soon as possible and in any event not less than 48 hours before the time appointed for holding of the SGM or any adjournment thereof. Completion and return of the form of proxy shall not preclude you from attending and voting at the SGM or any adjournment thereof if you so wish.

LETTER FROM THE BOARD

6. STATUS OF THE 2007 ACQUISITION

It was stated in the 2007 Announcement and the 2007 Circular that the 2007 Acquisition constituted a connected transaction for the Company as Mr. Ong is a substantial shareholder of Smart Ascent by virtue of his interest in Smart Ascent. In its letter of 20 September 2007 to the Company, the Stock Exchange indicated its views that Shareholders should have been given sufficient information on the 2004 Acquisition (including the view of the Stock Exchange that the 2004 Acquisition should have constituted a connected transaction and should have been subject to the relevant reporting, announcement and Independent Shareholders' approval requirements under Chapter 14A of the Listing Rules) to enable them to make a properly informed assessment of the relationship between the 2007 Acquisition and the 2004 Acquisition. At the request of the Stock Exchange and subject to the 2004 Acquisition having been approved and ratified by the Independent Shareholders, the Company is required to convene another special general meeting of the Company for the Independent Shareholders to re-consider and, if thought fit, to re-approve the 2007 Acquisition.

As disclosed in the 2007 Circular, completion of the 2007 Agreement is conditional upon the satisfaction or, as the case may be, waiver of the conditions precedent as stated therein, including but not limited to the Listing Committee of the Stock Exchange granting the approval for the listing of, and permission to deal in, the Consideration Shares issuable to Mr. Ong under the 2007 Agreement on the main board of the Stock Exchange, on or before 12:00 noon on 31 October 2007 or such later date (the "Long Stop Date") as the Group may agree. As at the Latest Practicable Date, the Group had not yet extended the Long Stop Date. It is the present intention of the Board to proceed with the acquisition of the remaining 49% interests in the share capital of Smart Ascent. The Directors will, however, after the ratification and approval of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby by the Independent Shareholders at the SGM, re-assess whether it is in the interests of the Group and the Shareholders (taken as a whole) (i) to extend the Long Stop Date and proceed with the acquisition of the remaining 49% interests in the share capital of Smart Ascent on the same terms and conditions (other than the Long Stop Date) as set out in the 2007 Agreement, or (ii) to re-negotiate with Mr. Ong on an arm's length basis on the terms and conditions for such acquisition.

There is no assurance that the Group will proceed with the acquisition of the remaining 49% interests in the share capital of Smart Ascent and, if proceed with, there is no assurance that such acquisition will be proceeded with on the same terms and conditions as set out in the 2007 Agreement. The Company will make further announcement in respect of the status of such acquisition pursuant to the Listing Rules as and when required. Shareholders and prospective investors should exercise caution when dealing in Shares.

7. RECOMMENDATION

The Independent Board Committee comprising all the independent non-executive Directors, namely Mr. Fang Lin Hu, Mr. Xue Jing Lun and Ms. Jin Song, has been established to advise the Independent Shareholders as to whether the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby, are fair and reasonable, on normal commercial terms, in the ordinary and usual course of business of the Group and in the interests of the Company and the Shareholders as a whole, and to advise the Independent Shareholders as to how to vote. Your attention is drawn to the advice of the Independent Board Committee set out in its letter on page 22 of this circular. Your attention is also drawn to the letter of advice from Somerley to the Independent Board Committee and the Independent Shareholders in respect of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby set out on page 23 to page 51 of this circular.

LETTER FROM THE BOARD

The Independent Board Committee, having taken into account the advice of Somerley, considers that the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby to be fair and reasonable and in the interests of the Company and the Shareholders as a whole. The Independent Board Committee therefore recommends the Independent Shareholders to vote in favour of the ordinary resolutions to ratify and approve the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby at the SGM.

8. ADDITIONAL INFORMATION

Your attention is drawn to the additional information set out in the appendices to this circular.

Yours faithfully,
By order of the Board
Extrawell Pharmaceutical Holdings Limited
Mao Yu Min
Chairman



EXTRAWEILL PHARMACEUTICAL HOLDINGS LIMITED

精 優 藥 業 控 股 有 限 公 司 *

(incorporated in Bermuda with limited liability)

(Stock Code: 00858)

21 May 2009

To the Independent Shareholders

Dear Sir or Madam,

**THE RATIFICATION ACTIONS FOR
THE ACQUISITION OF 51% INTEREST IN SMART ASCENT IN 2004**

CONNECTED AND DISCLOSEABLE TRANSACTIONS

We refer to the circular issued by the Company to its shareholders and dated 21 May 2009 (“**Circular**”) of which this letter forms part. Terms defined in the Circular have the same meanings when used in this letter unless the context otherwise requires.

We have been appointed by the Board to consider the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby, as to whether, in our opinion, they are fair and reasonable and in the interests of the Company and the Shareholders as a whole. Somerley has been appointed as the independent financial adviser to advise us and the Independent Shareholders in this respect.

We wish to draw your attention to the letter from the Board and the letter from Somerley as set out in the Circular. Having considered the principal factors and reasons considered by, and the advice of, Somerley as set out in its letter of advice, we consider that the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby are fair and reasonable and in the interests of the Company and the Shareholders as a whole. Accordingly, we would recommend the Independent Shareholders to vote in favour of the ordinary resolution to ratify and approve the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby at the SGM.

Yours faithfully,

For and on behalf of

Independent Board Committee

Mr. Fang Lin Hu Mr. Xue Jing Lun Ms. Jin Song

Independent non-executive Directors

* For identification purpose only

LETTER FROM SOMERLEY



SOMERLEY LIMITED
10th Floor
The Hong Kong Club Building
3A Chater Road
Central
Hong Kong

21 May 2009

*To: the Independent Board Committee
and the Independent Shareholders*

Dear Sirs,

CONNECTED AND DISCLOSEABLE TRANSACTION ACQUISITION OF A 51% INTEREST IN SMART ASCENT

INTRODUCTION

We refer to our appointment to advise the Independent Board Committee and the Independent Shareholders in connection with the ratification and approval of the acquisition by the Group of a 51% interest in Smart Ascent from Mr. Ong and Ms. Wu pursuant to the conditional sale and purchase agreement dated 3 March 2004 entered into between Ms. Wu and Mr. Ong as vendors and the Group as purchaser. Details of the above transaction are set out in the circular (the “Circular”) of the Company dated 21 May 2009 to its shareholders, of which this letter forms a part. Unless the context otherwise requires, capitalised terms used in this letter shall have the same meanings as those defined in the Circular.

The Independent Board Committee comprising all the three independent non-executive Directors, namely Mr. Fang Lin Hu, Mr. Xue Jing Lun and Ms. Jin Song, has been formed to advise the Independent Shareholders in respect of the 2004 Acquisition. We, Somerley Limited, have been appointed as the independent financial adviser to advise the Independent Board Committee and the Independent Shareholders in this regard.

Somerley has acted as the independent financial adviser to the independent board committee of Far East Pharmaceutical Technology Company Limited (“Far East Pharmaceutical”) as regards a mandatory unconditional cash offer (the “Offer”), details of which are contained in the composite offer and response document issued by Far East Pharmaceutical to its shareholders dated 17 October 2008. Far East Pharmaceutical changed its name to United Gene High-Tech Group Limited (“United Gene”) with effect from 3 March 2009. Dr. Mao Yumin, the chairman, executive director and a substantial shareholder of the Company, was a director and the controlling shareholder of the company which made the Offer. As at the Latest Practicable Date, Dr. Mao Yumin indirectly held approximately 63.4% equity interest of United Gene. Other than the above, Somerley Limited has had no business relationship with Dr. Mao Yumin, nor is it associated with the Company and the Vendors. Accordingly, we consider ourselves eligible to give independent advice on the 2004 Acquisition. Apart from normal professional

LETTER FROM SOMERLEY

fees payable to us in connection with our appointment as regards the Group's proposed acquisition of Smart Ascent, no arrangement exists whereby we will receive any fees or benefits from the Company or the Vendors.

In formulating our advice, we have relied on the information and facts supplied, and the opinions expressed, by the Directors and the management of the Group and have assumed that they are true, accurate and complete at the time they were made and will remain so up to the time of the SGM. We have reviewed the financial information on the Group, including its audited consolidated financial statements of the Group for the three years ended 31 March 2008 and its unaudited consolidated financial statements for the six months ended 30 September 2008; and on Smart Ascent, including its accountants' report (the "Accountants' Report") prepared by RSM Nelson Wheeler for the three years ended 31 March 2008 and the five months ended 31 August 2007 and 2008, the full text of which is contained in Appendix II to the Circular; the financial projections of the Smart Ascent Group from 1 October 2010 to 31 March 2015, which form the basis for the valuation; as well as the valuation report (the "Valuation Report") on the 100% equity interest in Smart Ascent Group dated 28 February 2009 (the "Valuation") prepared by Castores Magi Asia Limited (the "Valuer"), an independent valuer, and the medical expert report prepared by PKU Medical Investment Co., ("Medical Expert"), an independent medical expert. The reports prepared by the Valuer and the Medical Expert are contained in Appendix I and Appendix III respectively. We have also sought and received confirmation from the Directors that all material relevant information has been supplied to us and that no material facts have been omitted from the information supplied and opinions expressed to us. We have no reason to doubt the truth or accuracy of the information provided to us, or to believe that any material information has been omitted or withheld. We have relied on such information and consider that the information we have received is sufficient for us to reach our advice and recommendation as set out in this letter. However, we have not conducted any independent investigation into the business and affairs of the Group, including Smart Ascent and Fosse Bio, and are not experts in the medical application of insulin.

PRINCIPAL FACTORS AND REASONS CONSIDERED

In considering whether the terms of the 2004 Acquisition are fair and reasonable in so far as the Independent Shareholders are concerned, we have taken into account the principal factors and reasons set out below:

1. Summary of the 2004 Acquisition and the 2007 Acquisition

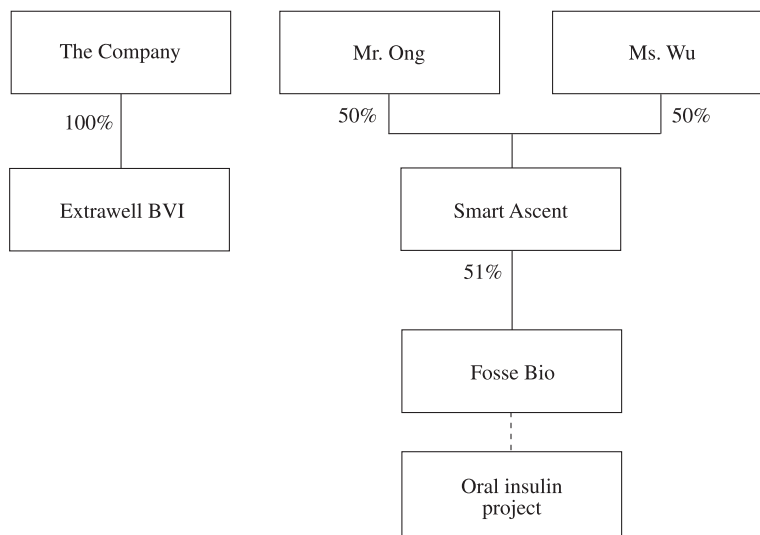
2004 Acquisition

On 3 March 2004, Extrawell BVI entered into the 2004 Agreement with the Vendors whereby it agreed to acquire a 51% interest in Smart Ascent, which was then equally owned by Mr. Ong and Ms. Wu. The principal asset of Smart Ascent is the holding of a 51% interest in Fosse Bio, which is principally engaged in the research and development of oral insulin with Tsinghua University, Beijing.

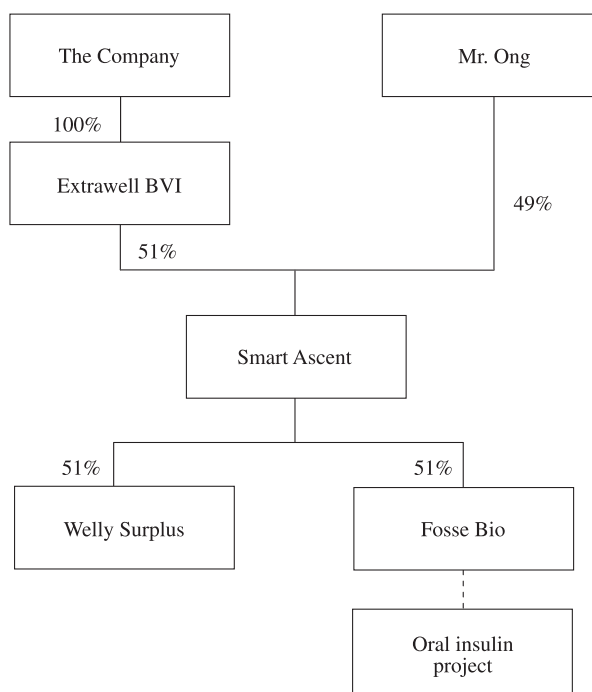
LETTER FROM SOMERLEY

Set out below is the shareholding structure of the Smart Ascent Group before and after completion of the 2004 Acquisition:

Before completion of the 2004 Acquisition



Current shareholding structure of the Group



Note: The other businesses of the Group which are not directly related to the 2004 Acquisition are excluded from the above shareholding structures of the Group.

LETTER FROM SOMERLEY

Consideration

Under the 2004 Agreement, the consideration (“2004 Acquisition Consideration”) paid by the Company to the Vendors for the 2004 Acquisition was HK\$73.0 million in cash, subject to adjustment. If the net asset value of Smart Ascent was less than zero as at completion of the 2004 Acquisition, the Vendors undertook to pay to Extrawell BVI an amount equal to that which would top up Smart Ascent’s unconsolidated net asset value to zero and the 2004 Acquisition Consideration would be adjusted accordingly pursuant to the 2004 Agreement. As a result, the 2004 Acquisition Consideration has been adjusted from HK\$73.0 million to approximately HK\$72.8 million.

Conditions precedent and completion

Completion of the 2004 Acquisition was conditional upon a number of conditions having been fulfilled, the major ones of which are set out in the paragraph headed “Conditions precedent and completion” in the “Letter from the Board” of the Circular. As set out therein, the 2004 Acquisition was subject to, if required, the Independent Shareholders’ approval of the 2004 Agreement and the transactions contemplated thereby and all other consents and acts required under the Listing Rules being obtained and completed or, as the case may be, the relevant waiver from compliance with any of such rules being obtained from the Stock Exchange. It was stated in the 2004 Announcement and the 2004 Circular that the 2004 Acquisition constituted a discloseable transaction of the Company pursuant to the Listing Rules and, apart from Mr. Ong being an independent non-executive Director prior to his resignation from the office on 2 August 2001, each of the Vendors and their respective associates were independent from and not connected with any of the Directors, chief executives or substantial shareholders of the Company or any of its subsidiaries or any of their respective associates. As a result, the Company did not at that time seek Independent Shareholders’ approval for the 2004 Acquisition prior to proceeding to completion. The 2004 Acquisition was completed on 17 August 2004, since then the results and assets and liabilities of the Smart Ascent Group have been consolidated into the accounts of the Group.

As disclosed in the Company’s clarification announcement dated 17 September 2007, it came to the attention of the Board that Mr. Ong is the son-in-law of Mr. Ho, a director of the Company until his resignation with effect from 12 March 2009, and Ms. Wu is the daughter-in-law of Mr. Ho. Under Rule 14A.11 of the Listing Rules, the definition of “connected person” includes a son-in-law and a daughter-in-law of a director whose association with the director is such that, in the opinion of the Stock Exchange, the transaction should have been subject to the connected transaction requirements under the Listing Rules. In its letter of 20 September 2007 to the Company, the Stock Exchange indicated its views that, taking into account the association of Mr. Ho with the Vendors as aforesaid, the 2004 Acquisition should have been subject to the relevant reporting, announcement and Independent Shareholders’ approval requirements under Chapter 14A of the Listing Rules. At the request of the Stock Exchange, the SGM will be held to seek the ratification and approval of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby by the

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Independent Shareholders. In the event that the Independent Shareholders do not approve ratification of the 2004 Acquisition, the Company intends to proceed to seek buyer(s) for the 51% interest in Smart Ascent.

2007 Acquisition

On 27 July 2007, Extrawell BVI entered into the 2007 Agreement whereby it agreed to acquire the remaining 49% interest in Smart Ascent from Mr. Ong. Consideration for the 2007 Acquisition is approximately HK\$768.9 million, to be satisfied by the Company allotting and issuing 300 million Consideration Shares at HK\$2.563 per share to Mr. Ong.

It was stated in the 2007 Announcement and the 2007 Circular that the 2007 Acquisition constituted a connected transaction for the Company as Mr. Ong is a substantial shareholder of Smart Ascent by virtue of his interest in Smart Ascent. Accordingly, the Company obtained Independent Shareholders' approval of the 2007 Acquisition on 20 September 2007. In its letter of 20 September 2007 to the Company, the Stock Exchange indicated its views that Shareholders should have been given sufficient information on the 2004 Acquisition (including the view of the Stock Exchange that the 2004 Acquisition should have constituted a connected transaction and should have been subject to the relevant reporting, announcement and Independent Shareholders' approval requirements under Chapter 14A of the Listing Rules) to enable them to make a properly informed assessment of the relationship between the 2007 Acquisition and the 2004 Acquisition. At the request of the Stock Exchange and subject to the 2004 Acquisition having been approved and ratified by the Independent Shareholders, the Company shall convene another special general meeting for the Independent Shareholders to re-consider and, if thought fit, to re-approve the 2007 Acquisition.

As disclosed in the 2007 Circular, completion of the 2007 Agreement is conditional upon the satisfaction or, as the case may be, waiver of the conditions precedent as stated therein, including but not limited to the Listing Committee of the Stock Exchange granting the approval for the listing of, and permission to deal in, the Consideration Shares on the main board of the Stock Exchange, on or before 12:00 noon on 31 October 2007 or such later date (the "Long Stop Date") as the Group may agree. As at the Latest Practicable Date, the Group had not yet extended the Long Stop Date. It is the present intention of the Board to proceed with the acquisition of the remaining 49% interest in the share capital of Smart Ascent. The Directors will, however, depending on the ratification and approval of the 2004 Acquisition, the 2004 Agreement and the transactions contemplated thereby by the Independent Shareholders at the SGM, re-assess whether it is in the interests of the Group and the Shareholders (taken as a whole) (i) to extend the Long Stop Date and proceed with the acquisition of the remaining 49% interests in the share capital of Smart Ascent on the same terms and conditions (other than the Long Stop Date) as set out in the 2007 Agreement, or (ii) to re-negotiate with Mr. Ong on an arm's length basis on the terms and conditions for such acquisition.

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2. Business and financial information of the Group

The Group is principally engaged in the manufacturing and sales of its own pharmaceutical products, as well as the marketing and distribution of imported pharmaceutical products, with PRC being the Group's major market. Besides the above, the Group has also been engaging in the development and commercialisation of oral insulin products since completion of the 2004 Acquisition. As the development of the Medicine is still in progress, currently no revenue is generated from that segment.

Set out below are the consolidated results of the Group for the three years ended 31 March 2008 and for the six months ended 30 September 2008 as extracted from the Group's 2007 and 2008 annual reports and the Group's 2008 interim report, which are prepared in accordance with the Hong Kong Financial Reporting Standards:

	For the six months ended 30 September 2008	For the year ended 31 March		
	2008	2008	2007	2006
	<i>HK\$'000</i>	<i>HK\$'000</i>	<i>HK\$'000</i>	<i>HK\$'000</i>
	<i>(unaudited)</i>	<i>(audited)</i>	<i>(audited)</i>	<i>(audited)</i>
Turnover	91,092	165,079	158,763	178,265
Cost of sales	<u>(69,583)</u>	<u>(113,004)</u>	<u>(109,996)</u>	<u>(108,450)</u>
Gross profit	21,509	52,075	48,767	69,815
	23.6%	31.5%	30.7%	39.2%
Other income	3,693	9,111	10,513	4,650
Selling and distribution expenses	(9,031)	(16,324)	(14,436)	(14,890)
Administrative expenses	(13,851)	(35,295)	(26,656)	(26,340)
Impairment losses	<u>—</u>	<u>(7,010)</u>	<u>(8,688)</u>	<u>(25,630)</u>
Profit from operations	2,320	2,557	9,500	7,605
Finance costs	<u>(2)</u>	<u>(164)</u>	<u>(197)</u>	<u>(908)</u>
Profit before tax	2,318	2,393	9,303	6,697
Income tax expense	<u>(2,948)</u>	<u>(15,728)</u>	<u>(369)</u>	<u>(2,510)</u>
(Loss)/profit for the period/year	<u><u>(630)</u></u>	<u><u>(13,335)</u></u>	<u><u>8,934</u></u>	<u><u>4,187</u></u>

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A breakdown of turnover and results by business segments is as follows:

	For the six months ended 30 September 2008	For the year ended 31 March		
	2008	2008	2007	2006
	<i>HK\$'000</i>	<i>HK\$'000</i>	<i>HK\$'000</i>	<i>HK\$'000</i>
	<i>(unaudited)</i>	<i>(audited)</i>	<i>(audited)</i>	<i>(audited)</i>
Turnover				
Manufacturing	25,285	42,049	43,275	51,714
Trading	65,807	123,030	115,488	126,551
Gene development	—	—	—	—
Oral insulin	—	—	—	—
	<u>91,092</u>	<u>165,079</u>	<u>158,763</u>	<u>178,265</u>
Segment results				
Manufacturing	1,728	(5,600)	1,121	(7,012)
Trading	5,761	15,773	17,175	33,257
Gene development	(212)	(186)	(232)	(341)
Oral insulin	(66)	(1,621)	(213)	(257)
	7,211	8,366	17,851	25,647
Interest income	654	2,841	1,789	1,001
Net unallocated expenses	(5,545)	(8,650)	(10,140)	(19,043)
Profit from operations	2,320	2,557	9,500	7,605
Finance costs	(2)	(164)	(197)	(908)
Profit before tax	2,318	2,393	9,303	6,697
Income tax expense	(2,948)	(15,728)	(369)	(2,510)
(Loss)/profit for the period/year	<u>(630)</u>	<u>(13,335)</u>	<u>8,934</u>	<u>4,187</u>

Turnover of the Group for the year ended 31 March 2007 of approximately HK\$158.8 million represented a decrease of approximately 10.9% over the figure recorded for the year ended 31 March 2006, and improvement was shown during the year ended 31 March 2008, with a slight increase of approximately 4.0% when compared to year ended 31 March 2007. Turnover for the six months ended 30 September 2008 amounted to approximately HK\$91.1 million, which represented an improvement when compared to the year ended 31 March 2008 on an annualised basis.

Gross profit percentage decreased from approximately 39.2% for the year ended 31 March 2006 to approximately 30.7% for the year ended 31 March 2007, then increased slightly again to approximately 31.5% for the year ended 31 March 2008. The significant decrease in gross profit

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percentage for the year ended 31 March 2007 was a result of the strengthening of PRC government policy restricting all government controlled hospitals from sourcing medicines other than through open tender during the year. As a result, sourcing agents placed more emphasis on pure price comparison. The Group reacted by lowering the sales price of its products, leading to a decrease in gross profit percentage. Gross profit percentage further declined to approximately 23.6% for the six months ended 30 September 2008.

Overall, segment results reduced significantly by approximately 30.4% from approximately HK\$25.6 million for the year ended 31 March 2006 to approximately HK\$17.9 million for the year ended 31 March 2007, which was mainly due to the above-mentioned policy change in the PRC. Segment results further reduced to approximately HK\$8.4 million for the year ended 31 March 2008, which mainly resulted from increased selling and distribution expenses and administrative expenses, as more resources were put into marketing and promotion activities with a view to increasing sales. Such increased resources, coupled with increased staff costs, resulted in poorer overall segment results for the year ended 31 March 2008. If compared on an annualised basis, segment results improved subsequently for the six months ended 30 September 2008, to approximately HK\$7.2 million, which was principally due to the recovery of the previous loss in the manufacturing segment.

The increase in administrative expenses for the year ended 31 March 2008 was resulted from the legal and professional fees incurred in relation to the compliance with the Listing Rule requirements as regards the ratification and approval of the 2004 Acquisition.

Impairment losses for the year ended 31 March 2006 were mainly in respect of property, plant, equipment and prepaid land lease payments (approximately HK\$10.7 million), trade receivables (approximately HK\$5.2 million) and goodwill (approximately HK\$1.0 million). Impairment losses for the year ended 31 March 2007 and 2008 were mainly related to trade receivables.

Income tax expenses increased substantially to approximately HK\$15.7 million for the year ended 31 March 2008. This arose from additional income tax provision in relation to the business operation in the PRC.

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Set out below are the consolidated balance sheets of the Group as at 31 March 2006, 2007 and 2008 and as at 30 September 2008 as extracted from the Group's 2007 and 2008 annual reports and the Group's 2008 interim report, which are prepared in accordance with the Hong Kong Financial Reporting Standards:

	As at 30 September 2008	As at 31 March 2008	2007	2006
	<i>HK\$'000 (unaudited)</i>	<i>HK\$'000 (audited)</i>	<i>HK\$'000 (audited)</i>	<i>HK\$'000 (audited)</i>
Non-current assets				
Property, plant and equipment	55,852	53,854	55,384	56,812
Prepaid land lease payments	14,406	14,251	13,977	13,850
Intangible assets	<u>285,624</u>	<u>285,782</u>	<u>287,722</u>	<u>287,898</u>
	355,882	353,887	357,083	358,560
Current assets				
Inventories	26,238	18,639	12,453	14,767
Trade receivables	86,617	97,948	98,571	86,177
Deposits, prepayments and other receivables (<i>note 2</i>)	62,467	58,697	55,372	56,851
Amounts due from minority shareholders	8	8	8	8
Pledged bank deposits	20,215	18,160	7,532	7,262
Bank and cash balances	<u>86,050</u>	<u>72,234</u>	<u>78,969</u>	<u>47,702</u>
	281,595	265,686	252,905	212,767
Current liabilities				
Trade and bills payable	10,676	13,023	9,657	8,323
Accruals and other payables	56,757	44,513	26,911	23,459
Interest-bearing borrowings				
— secured	—	—	19,542	4,630
Amount due to a director	—	—	3,257	—
Amount due to a minority shareholder (<i>note 1</i>)	32,404	32,404	32,404	32,404
Current tax liabilities	<u>19,400</u>	<u>16,654</u>	<u>1,631</u>	<u>1,641</u>
	119,237	106,594	93,402	70,457
Non-current liabilities				
Deferred tax liabilities	<u>102</u>	<u>102</u>	<u>102</u>	<u>102</u>
Net assets	<u><u>518,138</u></u>	<u><u>512,877</u></u>	<u><u>516,484</u></u>	<u><u>500,768</u></u>
Equity				
Share capital	22,900	22,900	22,900	22,900
Reserves	<u>278,212</u>	<u>274,020</u>	<u>276,019</u>	<u>257,761</u>
	301,112	296,920	298,919	280,661
Minority interests	<u>217,026</u>	<u>215,957</u>	<u>217,565</u>	<u>220,107</u>
	<u><u>518,138</u></u>	<u><u>512,877</u></u>	<u><u>516,484</u></u>	<u><u>500,768</u></u>

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Notes:

1. The balance included the Outstanding Purchase Price of approximately HK\$31.8 million, payable by Smart Ascent to Fordnew Industrial Limited (“Vendor of Fosse Bio”), in relation to the acquisition of the 51% interest in Fosse Bio by Smart Ascent (“Acquisition of Fosse Bio”) completed in November 2003, which would be further discussed below.
2. The balance included the Outstanding Amount which comprised the Outstanding Purchase Price of approximately HK\$31.8 million, and all legal costs, expenses and other liabilities which any of Smart Ascent or Extrawell BVI may incur (if any) in connection with the payment of the Outstanding Purchase Price, which the Vendors had jointly and severally undertaken and be responsible to pay in full such Outstanding Purchase Price for and on behalf of Smart Ascent if and when it becomes due and payable by Smart Ascent pursuant to the deed of transfer entered into by Smart Ascent for its acquisition of the 51% interest in the share capital of Fosse Bio.

Non-current assets of the Group as at 30 September 2008 mainly comprised intangible assets of approximately HK\$285.6 million. The Group’s intangible assets mainly included the carrying value of the technologies related to oral insulin in the sum of approximately HK\$284.3 million (the “Intangible Assets”), which was determined with reference to, among others, the consideration of approximately HK\$39.8 million (of which approximately HK\$31.8 million remained outstanding as at the Latest Practicable Date) for the Acquisition of Fosse Bio (“Fosse Bio Consideration”) and the consideration of approximately HK\$72.8 million for the 2004 Acquisition in respect of the purchase of a 51% interest in Smart Ascent by Extrawell BVI. Current assets of the Group as at 30 September 2008 represented mainly trade receivables of approximately HK\$86.6 million, bank and cash balances (including pledged bank deposits) of approximately HK\$106.3 million and the Outstanding Amount receivable from the Vendors of approximately HK\$31.8 million.

As at 30 September 2008, current liabilities included mainly accruals and other payables of approximately HK\$56.8 million, and amount due to a minority shareholder of approximately HK\$32.4 million. The approximately HK\$32.4 million mainly included the Outstanding Purchase Price of approximately HK\$31.8 million.

The approximately HK\$31.8 million Outstanding Purchase Price payable to the Vendor of Fosse Bio and the approximately HK\$31.8 million Outstanding Amount receivable from the vendors of Smart Ascent arose from Acquisition of Fosse Bio made by Smart Ascent prior to the 2004 Acquisition. Pursuant to the deed of transfer (the “Deed”) entered into between Smart Ascent and the Vendor of Fosse Bio, Smart Ascent acquired a 51% equity interest in Fosse Bio from the Vendor of Fosse Bio at a consideration totalling approximately HK\$39.8 million, which is payable in four instalments. The first and second instalments totalling approximately HK\$8 million had been paid. The third instalment of HK\$12 million shall be paid within 14 days from the production of original certificate of phase 3 clinical trials of the Medicine issued by SFDA for Smart Ascent’s inspection. The fourth instalment of approximately HK\$19.8 million shall be paid within 14 days from the production of original Certificate of New Medicine issued by SFDA for Smart Ascent’s inspection. The third and fourth instalments are recorded in the consolidated accounts of Smart Ascent as the amount due to a minority shareholder and remained outstanding as at the Latest Practicable Date. Pursuant to the 2004 Agreement, upon the Group acquiring Smart Ascent, the Vendors jointly and severally undertook to pay in full the outstanding Fosse Bio Consideration if and when it became due and payable. As a result, a corresponding amount of HK\$31.8 million was recorded as a receivable by the Smart Ascent Group. The Vendors have also undertaken jointly and

severally to pay in full all legal costs, expenses or other liabilities which any of Smart Ascent or Extrawell BVI may incur (if any) in connection with the payment of the Outstanding Purchase Price.

Shareholders shall note that in the respective “Independent Auditors’ Report” as contained in the Company’s 05/06, 06/07 and 07/08 annual reports, the then auditors of the Company highlighted the significant uncertainty relating to the recoverability of the Intangible Assets and the Outstanding Amount, which is largely contingent on the outcome of clinical trials of the Medicine. Shareholders are advised to read the full text of the respective “Independent Auditors’ Report” as contained in the above-mentioned annual reports of the Company.

3. Information on Smart Ascent

As mentioned above, the principal asset of Smart Ascent is the holding of a 51% interest in Fosse Bio which is developing the oral insulin project. Besides the holding of a 51% interest in Fosse Bio, Smart Ascent also holds a 51% interest in Welly Surplus, which will own a new manufacturing plant in the PRC for the manufacturing of the Medicine. Welly Surplus will act as the manufacturing and distribution arm of the Smart Ascent Group for the Medicine.

The oral insulin project

Background

Insulin is a kind of hormone which causes body cells to transform blood sugar into glycogen, which is stored as energy source. Diabetes develops when there is an abnormally high level of blood sugar. There are two major types of diabetes, Type 1 and Type 2 diabetes. Type 1 diabetes is characterised by the failure of the pancreas to produce insulin, which leads to a deficiency of insulin. Type 2 diabetes is characterised by the body’s inability to respond properly to the insulin produced by the pancreas.

Diabetes, especially Type 1 diabetes, can usually be treated by the intake of insulin. Unlike most of the other medication, insulin has not been successfully taken through the oral route in the past, and has to be taken through subcutaneous injection. As subcutaneous injection often causes pain and inconvenience to diabetic patients, there is research underway globally to develop new ways of insulin intake, including the oral route. However, there are two major obstacles in the research of oral insulin. Firstly, insulin, which is a protein, is digested and destroyed in the stomach and gut by digestive enzymes. Secondly, insulin cannot penetrate by itself through the wall of intestine into blood vessels.

Development of the Relevant Technologies and clinical trials

The development of the Relevant Technologies for producing oral insulin was first initiated in the 1990s and led by Mr. Zheng Chang Xue, a former professor of the Department of Biological Sciences and Biotechnology of the Tsinghua University, Beijing, and a minority shareholder of Fosse Bio. The Relevant Technologies involve the use of a fine micro-emulsion particle by combining protein with lipids, which can protect the protein from being digested and enable the protein to pass through the wall of digestive tract to the liver

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through portal vein. The liver is the major area in the body where the function of insulin takes place. Pre-clinical studies were performed to study the stability, absorption, transportation, capabilities and bioavailability of the Medicine.

Fosse Bio and Tsinghua University, Beijing, entered into the THU Collaboration Arrangement in 1998 in connection with the research and development of the Oral Insulin Products, including the Medicine. Pursuant to the THU Collaboration Arrangement, Fosse Bio will be entitled to commercialise the Relevant Technologies and to manufacture and sell the Oral Insulin Products in accordance with the provisions of the THU Collaboration Arrangement on an exclusive basis, and Tsinghua University, Beijing, is entitled to 1.5% of Fosse Bio's annual sales in return.

After satisfactory results from the pre-clinical studies, the formulation of the Medicine was approved by SFDA for clinical trials in 2003. The phase 1 clinical trial was designed to assess the safety of the drug, and was tested on a small number of healthy human testing subjects who did not suffer from diabetes. The phase 1 clinical trial was performed by a team of clinical experts in the National Pharmacology Research Base of the Peking Union Medical College Hospital (北京協和醫院). The phase 1 clinical trial was completed in early 2004.

Following the completion of the phase 1 clinical trial, the researchers of Fosse Bio proceeded to conduct the phase 2 clinical trial. The main objective of the phase 2 clinical trial was to study the bio-efficacy of the Medicine in terms of the level of reduction in blood sugar level. Unlike phase 1, patients suffering from diabetes were involved in the phase 2 clinical trial, which was conducted on a larger group of patients. During the trial, one group of patients was asked to take oral insulin while the control group was asked to use injected insulin. The phase 2 clinical trial, which was also led by the Peking Union Medical College Hospital (北京協和醫院) and involved a number of different medical centers in the PRC, commenced in early 2004 and was completed in the beginning of 2006.

One of the main conclusions from the clinical trials was that the intensity of oral insulin presence in blood vessels was approximately 7% of that of injected insulin, and the bio-efficacy of the Medicine (in terms of the reduction of blood sugar level) was approximately 25% of that of injected insulin. Such finding was queried by SFDA, which suggested that the bio-efficacy may be attributable to the psychological effect of the experiment towards diabetic patients. On the other hand, the Company was of the view that the Medicine was effective in reducing blood sugar level, and the low insulin intensity in blood vessels was mainly due to the fact that oral insulin travels to the liver directly through the portal vein (which drains blood from digestive system to the liver). The liver is the major location where the therapeutic effect and the catabolism of insulin take place, before the insulin is mostly digested (about 40% to 60% of the insulin should have been degraded in the liver) and released into the peripheral blood stream. As the oral insulin was degraded by liver cells during the process, the insulin released back to the blood vessels was substantially less than that of injected insulin, which resulted in a lower intensity of oral insulin being detected in blood vessels. On the other hand, injected insulin travels through the blood vessels to the liver, which leads to a relatively higher intensity of injected insulin being detected in blood vessels. The Medicine also tends to exhibit a long-acting characteristic of acting with higher stability and remaining in effect for a longer period than short-acting injected insulin.

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Originally it was expected that the Medicine could be regarded as a “Degree 4” drug, which includes drugs involving a change in delivery method (for example, oral intake rather than injection of insulin) in the human body, and may have been marketed in other countries around the world. When the Medicine was approved by SFDA for conducting phase 1 and phase 2 clinical trials in 2003, it was categorised by SFDA as a “Degree 2” drug, which include drugs involving a change in delivery method in the human body, and not yet marketed in any country around the world. Although phase 1 and phase 2 clinical trials have been completed with the reports for the results submitted to SFDA in August 2006, the Certificate of New Medicine is yet to be granted by SFDA, who indicated that an additional clinical trial was required before the final assessment and approval of the Medicine. In respect of the next phase of the clinical trial, SFDA imposed more stringent requirements which include a requirement for a larger sample group of patients, and the use of double-blind tests where neither the patients nor the researchers have knowledge on which patients belong to the experimental group (where patients will be given the Medicine) or the control group (where patients will be given placebos or other reference drugs), with a view to reducing experimental bias during the clinical trial.

The Company obtained the approval from SFDA to proceed with the next phase of the clinical trial pursuant to the approval document dated 30 April 2008 issued by SFDA, and expects the next phase of the clinical trial to commence in around late June of 2009. This phase of clinical trial involves a number of clinical trial centers located in different hospitals in major provinces of the PRC, and a larger sample size of patients, as compared to the previous phases of clinical trials. Currently, Fosse Bio is negotiating with the participating hospitals as regards details of the next phase of the clinical trial, which will be led by a reputable hospital based in Beijing, PRC. The Company expects that the next phase of the clinical trial will take approximately 6 to 7 months to complete, after which the data and statistics received from different clinical trial centers will be gathered and analysed for a further period of approximately 2 months. Following completion of the next phase of the clinical trial, results will be evaluated by SFDA, which is expected to last for approximately 6 months, before final approval. A Good Manufacturing Practice certificate has to be obtained before commencement of manufacturing of the Medicine.

Manufacturing facilities for the Medicine

In order to lower the operating risk for the development of the Medicine, the Group has agreed to co-operate with Sea Ascent as regards construction of a pharmaceutical manufacturing plant for the Medicine. On 19 October 2006, Welly Surplus, a 51% owned subsidiary of the Company, entered into a co-operation agreement (the “Cooperation Agreement”) with Sea Ascent Investment Limited (“Sea Ascent”), which is wholly owned by an independent third party named Mr. Wang Wei. Pursuant to the Cooperation Agreement, Sea Ascent will establish, through Joy Kingdom Industrial Limited (“Joy Kingdom”, a wholly owned subsidiary of Sea Ascent), a company named Jiangsu Prevalence Pharmaceutical Limited (“Jiangsu Prevalence”) to acquire a piece of industrial land situated in the Jiangsu Province, PRC and construct thereon a pharmaceutical manufacturing plant for the production of the Medicine. Sea Ascent also undertook to provide a loan of RMB40.0 million to Jiangsu Prevalence for acquisition of the land and construction of the plant and installation of necessary manufacturing facilities for the Medicine. In return, Sea Ascent will

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be entitled to a fee calculated at RMB6 cents for each capsule of Medicine produced, subject to a maximum of RMB180.0 million per year, for a period of six years commencing from the date on which the Medicine is launched for sales in the open market (“Initial Operating Period”). On the same day, Welly Surplus entered into a sale and purchase agreement (the “SP Agreement”) whereby it agreed to acquire from Sea Ascent (i) the entire equity interest in Joy Kingdom and (ii) the shareholders’ loan of RMB40.0 million from Sea Ascent, at a total consideration of approximately RMB40.0 million. A nominal amount of approximately RMB10,000 is payable upon completion of the SP Agreement, with the remaining balance payable within one month after the expiry of the Initial Operating Period. The Directors consider that through entering into the Cooperation Agreement and the SP Agreement, the Group may significantly lower the operating risk for development of the Medicine as the funding for acquisition of the land use rights, and construction of the manufacturing plant as well as installation of the manufacturing facilities would be advanced by Sea Ascent.

As at the Latest Practicable Date, the SP Agreement, and the construction of the plant, were yet to be completed. On 8 April 2009, Welly Surplus and Sea Ascent signed a confirmation, whereby both parties agreed to extend the long stop date of the SP Agreement from 30 November 2007 to 30 June 2010. We understand from management of the Company that the time-table for construction of the manufacturing plant for the Medicine and completion of the SP Agreement will tie to the approval process of the Medicine.

Expected future distribution channel for the Medicine

Should the Medicine be finally approved by SFDA, production and marketing would commence immediately. The Medicine can then be sold as a prescription drug in the PRC market. The Group has marketing and distribution channels in the PRC for the Group’s existing medical products, which can be utilised for marketing the Medicine. The Group expects that once the final approval for the Medicine is obtained, two distributors would be appointed in each of 30 major cities in the PRC for distribution of the Medicine initially. The Group has an experienced sales team who currently markets its products mainly through visits and seminars targeting doctors and other medical professionals. The Company considers that it would have sufficient resources to market and distribute the Medicine once SFDA approval is obtained.

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The following table summarises the consolidated financial results of Smart Ascent for the three years ended 31 March 2008 and for the five months ended 31 August 2008, which are prepared in accordance with the Hong Kong Financial Reporting Standards and extracted from the Accountants' Report, the full text of which is contained in Appendix II to the Circular:

	For the five months ended		For the year ended 31 March	
	31 August 2008	2008	2007	2006
	<i>HK\$'000</i>	<i>HK\$'000</i>	<i>HK\$'000</i>	<i>HK\$'000</i>
	<i>(audited)</i>	<i>(audited)</i>	<i>(audited)</i>	<i>(audited)</i>
Turnover	—	—	—	—
Administrative expenses	(159)	(502)	(215)	(278)
Loss before tax	(159)	(502)	(215)	(278)
Income tax expense	—	—	—	—
Loss for the period/year	<u>(159)</u>	<u>(502)</u>	<u>(215)</u>	<u>(278)</u>

Smart Ascent is an investment holding company. As mentioned above, as the oral insulin project is still in the clinical trial stage, no turnover was derived from this business. The administrative expenses represent general office and other expenses. Accordingly, Smart Ascent Group incurred net losses for the three years ended 31 March 2008 and for the five months ended 31 August 2008.

According to the shareholders' agreement of Fosse Bio, financing of the business of Fosse Bio should be met by borrowings or shareholders' loans contributed in proportion to their shareholdings in Fosse Bio, and upon the request of the Vendor of Fosse Bio, Smart Ascent shall provide interest-free loans to the other shareholders of Fosse Bio for onward lending as shareholders' loans to Fosse Bio. However, we are advised by the Company that a majority of the previous expenditures ("Previous Expenditures") incurred for the oral insulin project were not accounted for in the books of Fosse Bio (the results and financial position of which are consolidated into the audited accounts of Smart Ascent). This was because the minority shareholders of Fosse Bio had agreed to take up such Previous Expenditures, which included costs incurred for pre-clinical studies as well as the phase 1 and phase 2 clinical trials. The Company has obtained written confirmations from the minority shareholders of Fosse Bio that they would not claim back such expenditures from either Fosse Bio or Smart Ascent.

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The following table summarises the consolidated financial position of Smart Ascent as at 31 March 2006, 2007 and 2008 and as at 31 August 2008, which are prepared in accordance with the Hong Kong Financial Reporting Standards and extracted from the Accountants' Report:

	As at 31 August 2008 HK\$'000 (audited)	As at 31 March 2008 HK\$'000 (audited)	2007 HK\$'000 (audited)	2006 HK\$'000 (audited)
Non-current assets				
Intangible assets	281,473	281,473	281,473	281,473
Current assets				
Other receivables (<i>note 2</i>)	33,504	33,504	33,504	32,608
Bank and cash balances	<u>3</u>	<u>1</u>	<u>4</u>	<u>9</u>
	33,507	33,505	33,508	32,617
Current liabilities				
Accruals and other payables	390	560	203	238
Amount due to immediate holding company	4,430	4,100	3,958	2,816
Amount due to a minority shareholder (<i>note 1</i>)	<u>32,404</u>	<u>32,404</u>	<u>32,404</u>	<u>32,404</u>
	<u>37,224</u>	<u>37,064</u>	<u>36,565</u>	<u>35,458</u>
Net assets	<u><u>277,756</u></u>	<u><u>277,914</u></u>	<u><u>278,416</u></u>	<u><u>278,632</u></u>
Equity attributable to equity holders of Smart Ascent	141,060	141,218	141,693	141,891
Minority interests	<u>136,696</u>	<u>136,696</u>	<u>136,723</u>	<u>136,741</u>
Total equity	<u><u>277,756</u></u>	<u><u>277,914</u></u>	<u><u>278,416</u></u>	<u><u>278,632</u></u>

Notes:

- The balance included the Outstanding Purchase Price of approximately HK\$31.8 million, payable by Smart Ascent to the Vendor of Fosse Bio, in relation to the Acquisition of Fosse Bio, which was discussed above.
- The balance included the Outstanding Amount which comprised the Outstanding Purchase Price of approximately HK\$31.8 million, and all legal costs, expenses and other liabilities which any of Smart Ascent or Extrawell BVI may incur (if any) in connection with the payment of the Outstanding Purchase Price, which the Vendors had jointly and severally undertaken and be responsible to pay in full such Outstanding Purchase Price for and on behalf of Smart Ascent if and when it becomes due and payable by Smart Ascent pursuant to the deed of transfer entered into by Smart Ascent for its acquisition of the 51% interest in the share capital of Fosse Bio.

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The Intangible assets represented mainly the carrying value of the technologies related to oral insulin amounting to approximately HK\$281.5 million, which was determined with reference to, among others, the valuation report prepared by the Valuer in 2004, who valued the 100% equity interest in Fosse Bio at approximately HK\$279.8 million as at 31 January 2004. The net assets (excluding minority interests) of Smart Ascent Group remained at approximately HK\$141 million throughout the financial years or period under review.

Shareholders' attention is drawn to the content of report prepared by RSM Nelson Wheeler ("RSM") as contained in the Accountants' Report, in which RSM has expressed a disclaimer of opinion, largely based on the uncertain outcome of the results of the clinical trials as regards the Medicine. RSM also draws attention to the material uncertainty relating to the going concern basis, which arose because Smart Ascent has been making losses since incorporation.

4. Assessment of the 2004 Acquisition Consideration

As mentioned above, the Smart Ascent Group was loss making for the preceding three financial years, and the oral insulin project is yet to be commercialised. As such, price/earning multiple is not considered relevant in assessing the 2004 Acquisition Consideration. In the circumstances, we consider it appropriate to assess the 2004 Acquisition Consideration against the valuation of the economic value to be derived from commercialisation of the Medicine. Based on the estimated cash flow projections made by the management of the Company, the Valuer has valued the entire equity interest of Smart Ascent at approximately HK\$1,547.2 million as at 28 February 2009. The adjusted 2004 Acquisition Consideration of approximately HK\$72.8 million represents an approximately 90.8% discount to the valuation of approximately HK\$789.1 million attributable to a 51% interest in Smart Ascent as assessed by the Valuer.

5. Valuation of Smart Ascent

The Valuer has valued Smart Ascent on the basis of the financial projections of the Smart Ascent Group from 1 October 2010, which is the expected date of launch of the Medicine to the market, to 31 March 2015 (the "Forecast Period") prepared by the Company. We have discussed with the Valuer the methodology used for performing the Valuation and with the Company, in conjunction with the Valuer and the Medical Expert, on all major bases and assumptions used in the financial projections prepared by the Company.

The full text of the Valuation Report and the report from the Medical Expert are contained in Appendix I and Appendix III to the Circular respectively.

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Methodology and assumptions used for the Valuation

In the process of valuing Smart Ascent, the Valuer considered three valuation approaches, namely the market approach, cost approach and income approach. We concur with the Valuer that the market approach is not appropriate in the circumstances as, to the best understanding of the Valuer, there has been no public sale and purchase of similar business transactions in Hong Kong and the PRC. We also concur with the Valuer that the cost approach, which is normally suitable for a manufacturing company, is not appropriate for valuing an innovative project such as the one which Smart Ascent is embarking on. As a result, the income approach, which measures the present worth of the net economic benefit to be received and focuses on the income-producing capability of a company, is used by the Valuer for valuing Smart Ascent.

Under the income approach, the discounted cash flow (“DCF”) method was used by the Valuer, which estimates the market value of Smart Ascent by discounting the future free cash flows to be generated by Smart Ascent, including revenues and costs, to its present value.

Discount rate

A discount rate of 16.29% was used by the Valuer in discounting the future free cash flows generated by Smart Ascent. The discount rate was determined using the capital asset pricing model and applying the risk-free rate of 3.72%, beta of 1.277, risk premium of 3.58%, country risk premium of 4% and business risk premium of 4%.

Terminal value

Of the HK\$1,547.2 million valuation on the entire interest of Smart Ascent, approximately 66.4% is attributable to the terminal value which was calculated by discounting the forecast cash flow as from 1 April 2015, by then the economic return from the oral insulin project is expected to have reached a more stable level, and assumes a perpetual growth rate of 2% per annum.

We notice that the patent granted to Fosse Bio and Tsinghua University, Beijing, in respect of the Relevant Technologies to be used for manufacturing the Medicine will expire in April 2021. In assessing the terminal value, the Valuer has assumed a perpetual growth even after expiry of the patent. The Valuer took the view that there is no concrete basis to assume non-renewal of the patent after expiry. The Company considers that even if the patent of the Relevant Technologies cannot be renewed after April 2021, the Company would by then have a fully established marketing and sales channel for the Medicine and should be able to enjoy competitive advantages over the new market entrants.

As it is not possible to quantify the effect of patent expiry and for the sake of prudence, we have ourselves prepared a scenario analysis which also includes a case prepared on the assumption that there would be no free cash flow after the expiry of the patent. Please refer to the sub-section below headed “Sensitivity analyses” for our further analysis on the effect of this (*Scenario (B)*) and other changes to different assumptions adopted in the original financial projections prepared by the Company.

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Discount for lack of marketability (“LOM”)

Smart Ascent is a closely held company and its equity is not readily marketable as a public listed company. The Valuer has therefore applied a LOM discount of 35% to the net present value of the future free cash flows. In determining the 35% LOM discount, the Valuer has made reference to the previous research and studies on the average discounts applicable to closely held companies, which ranged from 10% to 50%. When a company is valued by reference to free cash flows over a long period, a LOM may not be as relevant as in some other cases. However, we concur with the Valuer’s approach from the point of view of conservatism or “buffer” and consider that the 35% LOM discount is reasonable in the circumstances.

Major bases and assumptions used in the financial projections

Timing

According to the Medical Expert, the Medicine is currently categorised by SFDA as “Degree 2” drug, which include drugs involving a change in delivery method (for example, oral intake rather than injection of insulin) in the human body, and not yet marketed in any part of the world. Based on the progress and results from the clinical trials up-to-date, the Company believes there would be no major obstacle in completing the next phase of the clinical trial for the Medicine and obtaining the final approval from SFDA for production and distribution of the Medicine in the PRC. Based on the above, the Company estimates that the commencement of commercial production and distribution of the Medicine will be in October 2010, i.e. approximately 19 months from the date of the Valuation. Based on the Medical Expert’s report, this seem reasonable to us, but the Medicine has a history of delays to its commercialisation. We have therefore performed a sensitivity analysis on the effect of a delay in commercial launch of the Medicine (*Sensitivity analysis (1)*).

Diabetic population and market share in the PRC diabetic market

In estimating the revenue to be generated from marketing the Medicine in the PRC, the Company includes the whole diabetic population in the PRC as its target market, i.e. including the Type 1 diabetes and Type 2 diabetes. As Type 1 diabetics cannot produce insulin by themselves, they must take insulin to restore the insulin level in their bodies and oral insulin can be effective in this respect. On the other hand, the treatment of Type 2 diabetes can be a combination of continuous diet, exercises and the use of oral anti-diabetic drugs (“OADs”), which aim to lower glucose level in the human body. The Company is of the view that insulin is a preferred treatment to OADs for Type 2 diabetes as OADs are considered to create more adverse side-effects to patients. Based on the above, the Company believes that the prospective target customers can include both Type 1 and Type 2 diabetics in the PRC and this seems reasonable.

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The Company estimates a diabetic population (including Type 1 and Type 2 diabetes) of 58 million in the PRC when the Medicine commences commercial sales in October 2010, with a growth of 0.5 million annually afterwards, which roughly translates to 1% annual growth. There is no market consensus or official statistics on the size of the diabetic population in PRC. Based on a research report published by 中華醫學會糖尿病學分會 in November 2008, there is currently a diabetic population of approximately 60 million. Although the Medical Expert is of the view that the estimation of 60 million diabetic population in the PRC is more up-to-date and relevant, research published in other relevant articles show that there is an expected annual growth of 1.2 million diabetic population in the PRC, but with a lower starting estimated population of approximately 50 million.

The Company has made the following assumptions on the percentages and subsequent growth of market share in the Type 1 diabetic population and Type 2 diabetic population respectively in estimating the market share of the Medicine in the PRC diabetic population:

For the year ended:	Market share in:	
	Type 1 diabetic population	Type 2 diabetic population
31 March 2011	0.5%	1.5%
31 March 2012	0.8%	1.8%
31 March 2013	1.2%	2.4%
31 March 2014	1.5%	3.2%
31 March 2015	1.8%	4.0%

In estimating the market share of the Medicine, the Company has taken into account the market shares of existing competitors in the insulin market in the PRC, as well as the growth potential of the market share with reference to the management's knowledge of penetration of other new medicines in the PRC.

Overall, we consider the Company's estimation in this regard reasonable. However, for illustrative purpose, we have performed a sensitivity analysis below on each of the effect of (i) a lower estimation of diabetic population in October 2010 (*Sensitivity analysis (4)*) and (ii) a slower growth in market share of the Medicine in the PRC (*Sensitivity analysis (2)*) to the Valuation.

Pricing

The Company estimated a price of RMB2.4 (or approximately HK\$2.73) per capsule (with 50 units of insulin). Based on the findings from the previous clinical trials, the management estimates that the suitable level of intake of the Medicine for a Type 1 and Type 2 diabetics per day are 200 units and 100 units of insulin intake respectively, which is equivalent to 4 capsules and 2 capsules of the Medicine respectively.

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In determining the pricing of the Medicine, which is the wholesale distribution price of the Medicine, the Company has taken into account the market acceptability of the estimated retail price of the Medicine. In the opinion of the management, distributors may accept a lower margin for an unprecedented new drug like oral insulin which is generally believed to have great market potential. In assessing the market acceptability of the estimated retail pricing, the management has referred to the pricing of injected insulin and OADs currently available in the PRC market.

Cost of sales and other expenses

Cost of sales in the financial projections is separated into variable and fixed components, and the variable components contributed to the majority of the cost of sales. Variable component in cost of sales include the cost of local insulin which is the main component of the Medicine, and other chemical components. The variable component also includes variable processing costs incurred in the production of the Medicine, as well as the RMB6 cents per capsule manufactured payable to Sea Ascent as mentioned in the section above headed “Information on Smart Ascent”. Fixed costs include principally land and property taxes and other fixed factory overheads such as labour cost. We have performed a sensitivity analysis on the impact of a lower unit selling price and a higher unit cost on the Valuation (*Sensitivity analysis (3)*).

Expense items are principally marketing and distribution expenses and administrative expenses. It is expected that these expenses will largely increase in proportion to the increase in revenue. Main item of marketing and distribution expenses is the amount payable to Tsinghua University, Beijing, which will be calculated based on 1.5% of annual sales of the Medicine as agreed under the THU Collaboration Arrangement. Other items include finance costs, pre-operating expenses, amortisations and income tax.

The Medical Expert has expressed in its report that it has reviewed the bases and assumptions used in the Valuation, and considered such bases and assumptions fair and reasonable.

Sensitivity analyses

As any financial forecast is based on a number of assumptions which are likely to be different from the actual outcome, we have performed various sensitivity analyses to assess the effect of altering the assumptions on the Valuation. We have performed the sensitivity analyses under two scenarios: (i) scenario (A) assumes a perpetual growth rate of 2% per annum beyond the Forecast Period, when the financial projections are expected to start demonstrating a stable growth. This is the assumption adopted in the Valuation Report; (ii) scenario (B) assumes a growth rate of 2% per annum beyond the Forecast Period until the expiry of the patent of the Relevant Technologies in April 2021, after which there would be no free cash flow to Smart Ascent. The sensitivity analyses are intended for reference only, and any variation could be different from and could exceed or fall short of the adjustments given. Shareholders should note in particular that (i) the sensitivity analyses are not intended to be exhaustive and are limited to the impact of changes in the timing of launch of the project to the market, the market share of the Medicine in the PRC, unit selling price and unit cost, and the diabetic population in the PRC, and (ii) the financial projections are subject

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to further and additional uncertainties generally. The actual financial performance of the Smart Ascent Group may differ materially from the financial projections as well as the sensitivity analyses, and is dependent on market conditions and other factors that are beyond the control of the Smart Ascent Group. Please refer to the section below headed “Risk Factors” for further discussion of the principal risk factors in connection with the 2004 Acquisition.

Set out below is a summary of each of the sensitivity analyses that we have performed, and the valuation of the 51% equity interest of Smart Ascent under each sensitivity analysis, assuming other bases and assumptions remain unchanged:

Sensitivity analysis based on: <i>(see further details in the paragraphs below)</i>	Adjusted valuation of 51% interest in Smart Ascent based on:	
	Perpetual growth rate of 2% per annum Scenario (A) HK\$ million	No free cash flow after expiry of the patent for the Relevant Technologies Scenario (B) HK\$ million
(1) timing of launch of the project to the market	583.6	354.4
(2) market share of the Medicine in the PRC	603.2	426.5
(3) unit selling price and unit cost	602.3	393.0
(4) diabetic population in the PRC	674.5	470.2
Combination of sensitivity analyses:		
(1) and (2): delay in product launch and reduction in market share	446.1	276.2
(1) and (4): delay in product launch and smaller diabetic population	498.8	302.4
(2) and (3): reduction in market share and unit selling price, and increase in unit cost	448.4	293.8
(2), (3) and (4): reduction in market share and unit selling price, increase in unit cost and smaller diabetic population	379.7	248.0
Worst case scenario (all of the above occurring)		154.2

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Sensitivity analysis (1): timing of launch of the project to the market

In this sensitivity analysis, we have assumed that commencement of commercial production of the Medicine would be delayed by two years to October 2012. The adjusted valuations based on sensitivity analyses (1)(A) and (1)(B) are approximately HK\$583.6 million and HK\$354.4 million respectively.

Sensitivity analysis (2): market share of the Medicine in the PRC

In this sensitivity analysis, we have lowered the market share of the Medicine as estimated by the Company as follows:

For the year ended:	Market share in:	
	Type 1 diabetic population	Type 2 diabetic population
31 March 2011	0.5%	1.5%
31 March 2012	0.5%	1.5%
31 March 2013	0.75%	2.0%
31 March 2014	1.0%	3.5%
31 March 2015	1.25%	3.0%

The adjusted valuations based on sensitivity analyses (2)(A) and (2)(B) are approximately HK\$603.2 million and HK\$426.5 million respectively.

Sensitivity analysis (3): unit selling price and unit cost

In this sensitivity analysis, we have adjusted downward the unit selling price of the Medicine from RMB2.4 per capsule, starting with RMB1.8 per capsule and with a progressive increment in selling price throughout the Forecast Period to RMB2.4 per capsule, and adjusted upwards the unit cost from RMB1 to RMB1.1:

For the year ended:	Unit selling price	Unit cost
	(RMB)	(RMB)
31 March 2011	1.8	1.1
31 March 2012	1.8	1.1
31 March 2013	2.0	1.1
31 March 2014	2.2	1.1
31 March 2015	2.4	1.1

The adjusted valuations based on sensitivity analyses (3)(A) and (3)(B) are approximately HK\$602.3 million and HK\$393.0 million respectively.

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Sensitivity analysis (4): diabetic population in the PRC

In this sensitivity analysis, we have assumed that the initial diabetic population in the PRC is 50 million instead of 58 million, with the annual growth thereafter to be 0.5 million, which is the same as the Company's estimation. The adjusted valuations based on sensitivity analyses (4)(A) and (4)(B) are approximately HK\$674.5 million and HK\$470.2 million respectively.

Combination of sensitivity analyses

Apart from the stand-alone sensitivity analyses, we have constructed 4 different combinations of the above sensitivity analyses to illustrate scenarios where more than one of the above varied assumptions happen at the same time. Based on the results of the 4 combinations, the adjusted valuations ranged from approximately HK\$248.0 million to approximately HK\$498.8 million.

Worst case scenario

In the worst case scenario, we have incorporated all the adjustments made in scenarios 1 to 4, and assume no free cash flow following the expiry of the patent of the Relevant Technologies in April 2021 (i.e. scenario (B)). The adjusted valuation based on the worst case scenario is approximately HK\$154.2 million.

We note that the adjusted valuations under all the above sensitivity analyses, including the worst case scenario, are higher than the consideration of HK\$72.8 million for the 2004 Acquisition. On this basis, we are of the view that while there is a wide range of values which can be calculated, it is difficult, five years later with some significant degree of progress having been made, to construct a plausible scenario where the consideration under the 2004 Acquisition paid by the Group exceeds the Valuation.

6. Financial effects

Income statement and balance sheet

Following the completion of the 2004 Acquisition in August 2004, Smart Ascent and Fosse Bio became non-wholly owned subsidiaries of the Group. Accordingly, their results and financial position have been consolidated into the Group's financial statements since then. Consequently, if the 2004 Acquisition is ratified and approved by the Independent Shareholders at the forthcoming SGM, it would not give rise to any change to the results and financial position of the Group.

On an ongoing basis, the carrying values of the technical know-how in relation to the Relevant Technologies of HK\$284.3 million is subject to annual impairment test, and the recoverability of the Outstanding Amount receivable from the Vendors as discussed in the above paragraph is also subject to regular review. A provision for impairment loss may result should the clinical trials or the launch of the Medicine be unsuccessful. However, such impairment loss would be a "non-cash" charge.

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The commercial launch of the Medicine to the PRC market is expected to be in October 2010. After this time, the Company expects to record revenue and positive cash flows from sales of the Medicine, which will be reflected in the financial performance and position of the Group as a whole.

Cash flow

The Company estimates that Fosse Bio will incur a further approximately HK\$16 million of research and development expenses in relation to the next phase of the clinical trial, and a further approximately HK\$6 million for pre-marketing efforts before the commencement of commercial production and distribution of the Medicine. According to the shareholders' agreement of Fosse Bio, upon the request of the Vendor of Fosse Bio, Smart Ascent shall provide interest-free loan to Fosse Bio in proportion to its shareholding in Fosse Bio and/or provide interest-free loan to the other shareholders of Fosse Bio for onward lending to Fosse Bio for expenses relating to the clinical trials. Given that the free bank and cash balance of the Group amounted to approximately HK\$81.2 million as at the Latest Practicable Date, we consider that the additional expenditure required for the oral insulin project can be funded by the Group from its internal resources.

In case the 2004 Acquisition is not ratified and approved at the SGM, the Company intends to dispose of its 51% interest in Smart Ascent. In this case, Smart Ascent and Fosse Bio would no longer be consolidated into the accounts of the Group. However, since the terms of such a disposal cannot be known at the moment, the financial impact of any such disposal cannot be ascertained at this stage.

7. Risk factors

Set out below are the principal risk factors in connection with the 2004 Acquisition which we have considered during our assessment of the fairness and reasonableness of the 2004 Acquisition as well as the bases and assumptions used in the Valuation:

Final approval for production and distribution not yet obtained

As discussed in the above section headed "Information on Smart Ascent", Fosse Bio is preparing the next phase of the clinical trial, which is subject to evaluation and queries by SFDA after completion. It is still possible that the Medicine will fail to obtain SFDA approval. Alternatively, SFDA may impose additional requirements or raise queries on the clinical trial, which may create further hurdles for the final approval. Since the 2004 Acquisition was completed, the Company appears to have made steady progress, including the completion of pre-clinical studies and the completion of phases 1 and 2 of clinical trials, although at a slower pace and with more 'hurdles' than originally expected. Nevertheless, the timing of final approval is difficult to assess.

Fosse Bio is also required to obtain a number of licences, certificates and permits from the relevant regulatory authorities in the PRC before formal production and distribution of the Medicine can begin. These include, among others, the Certificate of New Medicine (新藥證書) and the Good Manufacturing Practice certificate. These licences, certificates and permits may also be subject to periodic renewal requirements.

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Should Fosse Bio fail to obtain all necessary approvals from the relevant authorities, it may not be able to commence the production and distribution of the Medicine in the PRC, which would have material and adverse impact on the business and financial results of Fosse Bio, and in turn the Group's business and financial results. The Group may also have to write-off or suffer impairment on the carrying values of the technological know-how in relation to the Relevant Technologies, which amounted to approximately HK\$284.3 million as at 30 September 2008.

Funding requirement

As discussed in the above section headed "Financial effect", the Company estimates that Fosse Bio will incur a further approximately HK\$16 million of research and development expenses in relation to the next phase of the clinical trial, and a further approximately HK\$6 million for pre-marketing efforts before the commencement of commercial production and distribution of the Medicine. Should the actual development and pre-marketing expenses turn out to be higher than the above amounts and the Group is unable to inject sufficient funding to support further development of the Medicine due to working capital needs from its existing operations, the oral insulin project may not be able to be completed and commercialised successfully.

Manufacturing and distribution

As at the Latest Practicable Date, the manufacturing plant for the Medicine was still under construction. Other than a small scale production of the Medicine for clinical trials, the Group has not yet commenced production of the Medicine. Should the manufacturing techniques prove to be faulty or a major processing reengineering has to be performed before mass scale production, a significant delay to the timing of the launch of the Medicine would be likely.

The Group expects to appoint two distributors in each of 30 major cities in the PRC for distribution of the Medicine during the initial stage. In case such appointment of distributors cannot be completed on time, or disagreement on terms of appointment arise, or the sales channels prove to be too weak to promote sales of the Medicine, the target market share of the Medicine may not be reached.

Market acceptance and competition

It is assumed in the financial projections of Smart Ascent that Fosse Bio would gain an increasing market share during the Forecast Period from October 2010 to March 2015. However, there can be no assurance that the Medicine can gain enough market acceptances in the PRC diabetic market in order to achieve the projected revenue. The level of market penetration, sales and pricing can only be broad estimates at this stage. In case it cannot be demonstrated in the next phase of the clinical trial that the Medicine has any sustained improvement over existing treatments, Fosse Bio may not be able to gain enough market acceptances to support the estimated revenue.

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In assessing the acceptance of the new Medicine to be launched to the market, diabetic patients may also make reference to the pricing of the Medicine as compared to other existing products. If the pricing assumption made by the Group proves too optimistic, target diabetics may stay with their existing drugs without switching to the Medicine.

Snags can occur regarding the effectiveness of the drug and the emergence of side-effects when it comes into wide use. There are precedent cases of seemingly promising new drugs which failed to become established. Exubera, which was an inhalable insulin introduced by Pfizer Incorporated and available in the United States from 2006 to 2007, was withdrawn from the market after it failed to gain acceptance among diabetic patients.

If the Medicine is approved and introduced successfully, there appears to be a large potential market of diabetes sufferers in the PRC. Nevertheless, rival products could emerge and, as noted above, the sales price is yet to be tested in the market. Competition from existing insulin products in the PRC market may also create uncertainty as to the projected revenue of Fosse Bio. Although the Company considered that the Medicine is likely to be the first oral insulin to be distributed in the PRC upon successful commercialisation, potential customers might still consider different factors when choosing among diabetic drugs available in the market, which include pricing, branding and reputation, availability, convenience of use and certain other factors. Besides, the possibility of oral insulin with similar technologies or insulin with other delivery methods being developed, or existing OADs available in the PRC market being sold more aggressively by competitors, may also impact the financial results of Fosse Bio.

Expiry of patent of the Relevant Technologies

The patent issued by the PRC authorities for the Relevant Technologies will expire in April 2021. At that time, the drug could become “generic”, with a lower profit margin. It is uncertain whether the patent can be renewed for a further period of time. As discussed in the section above headed “Valuation of Smart Ascent”, the appraised value of Smart Ascent is based on a perpetual growth in free cash flows to Smart Ascent at 2% per annum after the Forecast Period. Should Fosse Bio fail to renew the patent after its expiry, there may be a significant drop in revenue.

Product concentration

The financial projections of the oral insulin project prepared by the Company are based solely on the sales of the Medicine, which account for 100% of the revenue to be generated by Fosse Bio. In the event that the Medicine is not successfully commercialised in the PRC market, or the sales price / sales volumes of the Medicine do not reach the projected amounts, the Smart Ascent Group’s total sales would be materially and adversely affected.

Fluctuations in cost of sales

According to the financial projections, the cost of the main component of the Medicine, insulin powder, accounts for approximately 60% of the total cost of sales. The price of insulin powder and other cost components are subject to a number of factors such as supply

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and demand, and the economic environment in the PRC at the time. The gross margin of Fosse Bio may be adversely impacted if the purchase price of insulin powder or other components rises significantly.

Product liability

Fosse Bio could face material claims arising from any alleged harmful effect of the Medicine. There is no assurance that any product liability claim brought against the Group in respect of the Medicine would not have an adverse effect on Fosse Bio's business operations and financial results and position, and accordingly the Group's business operations and financial results and position.

DISCUSSION AND ANALYSIS

Diabetes is a major disease afflicting worldwide populations and appears to be increasing with affluence. Consequently, major pharmaceutical companies, both in the developed and developing world, have endeavoured to find a more convenient delivery method for insulin, the main drug used to combat diabetes, than the traditional injections. We have therefore approached the possibility that a relatively small group such as the Company should have discovered such a method with a degree of scepticism.

Nevertheless, the Company, through Fosse Bio which has been collaborating with Tsinghua University, Beijing, does seem to have made significant progress towards this goal. The THU Collaboration Arrangement was entered into among parties including Fosse Bio and Tsinghua University, Beijing, in 1998 and after satisfactory pre-clinical studies, the Medicine was approved for clinical trials in 2003. Phase 1 clinical trial was completed in 2004 and phase 2 in 2006. As described above, the results of phase 1 and phase 2 clinical trials broadly showed that the Medicine had a positive effect. However, SFDA did not approve the Medicine but ordered a further clinical trial, and required more stringent trial requirements including a larger sample of patients and a "double-blind" technique. This will take up to further 6 to 7 months and cost approximately HK\$16 million. Consequently, Fosse Bio's method is not yet "home and dry". Indeed, it is still possible that the required SFDA approval will not be obtained.

In addition to SFDA approval of the Medicine, a Good Manufacturing Practice certificate is required. Manufacturing arrangements have been agreed with Jiangsu Prevalence but are not yet in operation. There is also the task of effective marketing and distribution of the Medicine to be undertaken, including establishing the pricing policy.

The independent Valuer has carried out the Valuation based on projected cash flows assuming the SFDA approvals have been obtained and sales begin by October 2010. The basis and assumptions for the financial projections were made by the Company and we have discussed the basis and assumptions with the Medical Expert and the Valuer.

The Valuer used a discount rate of approximately 16% to discount future net cash flows to be generated by the Smart Ascent Group. In our view, this discount rate, which includes a 4% country risk premium and a 4% business risk premium, is relatively high. In addition to the Valuation, we have utilised the Valuer's model to vary one or more of the assumptions used to less favourable ones. We note that the adjusted valuations under all the sensitivity analyses, including a "worst case scenario" of approximately HK\$150 million, are higher than the consideration of HK\$72.8 million for the 2004

LETTER FROM SOMERLEY

Acquisition. On this basis, we are of the view that while there is a wide range of values which can be calculated, it is difficult, five years later with some significant degree of progress having been made, to construct a plausible scenario where the consideration under the 2004 Acquisition paid by the Group exceeds the Valuation.

Significant risks for the successful execution of the project remain, as summarised in section 7 above. However, as mentioned above, the valuation of the 51% interest in the Smart Ascent Group is higher than the 2004 Acquisition Consideration even on unfavourable assumptions, and Fosse Bio have achieved positive results for the two phases of clinical trials that have been completed so far. On this basis, we consider it in the interest of the Independent Shareholders to ratify and approve the 2004 Acquisition so as to reserve the Group's position to benefit from opportunities that may be brought by the commercialisation of the Medicine.

RECOMMENDATION

Having taken into account the above principal factors, we consider that the 2004 Acquisition is on normal commercial terms which are fair and reasonable so far as the Independent Shareholders are concerned. We also consider that the entering into of the 2004 Agreement is in the ordinary and usual course of business of the Company and in the interests of the Company and its shareholders as a whole. We therefore advise the Independent Board Committee to recommend, and ourselves recommend, the Independent Shareholders to vote in favour of the ordinary resolution to be proposed at the SGM to approve and ratify the 2004 Acquisition.

Yours faithfully,
for and on behalf of
SOMERLEY LIMITED
M. N. Sabine
Chairman

1. VALUATION REPORT

The following is the text of the valuation report dated 21 May 2009 from Castores Magi Asia Limited, an independent valuer, in respect of its valuation on the business carried out by Smart Ascent and its subsidiaries as at 28 February 2009, prepared for the purpose of incorporation in this circular.

嘉漫亞洲有限公司
CASTORES MAGI ASIA LIMITED
BUSINESS AND INTANGIBLE ASSET APPRAISAL
INVESTMENT PROJECT ADVISORY SERVICES

CASTORES

MAGI

Suite 211
China Insurance Group Building
141 Des Voeux Road Central
Hong Kong

21 May 2009

The Directors
Extrawell Pharmaceutical Holdings Limited
Room 3409-10,
34th Floor,
China Resources Building,
26 Harbour Road,
Wanchai,
Hong Kong.

Dear Sirs,

In accordance with the instructions of Extrawell Pharmaceutical Holdings Limited (hereinafter known as “the Company”), we have made an appraisal of the Market Value of a 100% equity interest of Smart Ascent Limited (hereinafter known as “Smart Ascent”) and its subsidiaries[#] (altogether hereinafter known as the “Smart Ascent Group”), as at 28 February 2009 (hereinafter known as “the Valuation Date”).

The purpose of this appraisal is to formulate and express an independent opinion on the Market Value of Smart Ascent Group as at the Valuation Date on the premise of going concern. The term “Market Value” as used herein is defined as “the estimated amount for which an asset should exchange on the date of valuation between a willing buyer and a willing seller in an arm’s length transaction after proper marketing wherein the parties had each acted knowledgeably, prudently, and without compulsion”. We understand that the use of our work product will not supplant other due diligence which you should conduct in reaching business decisions for Smart Ascent. Our work is designed solely for public disclosure purposes. There are no other purposes are intended or should be inferred.

[#] Smart Ascent owns as to 51% equity interest of Fosse Bio-Engineering Development Limited and 51% equity interest of Welly Surplus Development Limited

Introduction

Smart Ascent was incorporated in Hong Kong with limited liability and is a 51% indirectly-owned subsidiary of Extrawell Pharmaceutical Holdings Limited, a company listed on The Stock Exchange of Hong Kong Limited. As at the Valuation Date, Smart Ascent possesses 51% equity interest of Fosse Bio-Engineering Development Limited (hereinafter known as “Fosse Bio”) and 51% equity interest of Welly Surplus Development Limited (hereinafter collectively known as the “Welly Surplus”). Smart Ascent Group principally engages in the development and commercialisation of Oral Insulin Enteric-Coated Soft Capsule (hereinafter known as “Oral Insulin”).

Fosse Bio has collaborations with Tsinghua University for the research and development of the use of oral insulin, and shall have the exclusive right to commercialize the technologies relating to the use of Oral Insulin, manufacture and sell it on exclusive basis. On the other hand, Welly Surplus will serve as the manufacturing and distribution arm of Smart Ascent.

Diabetes is disease in which the body does not produce or properly use insulin, which causes high levels of glucose in the blood. There are two types of Diabetes: Type 1 diabetes - human body suffering insulin deficiency (little or no insulin); Type 2 diabetes — human body suffering insulin resistance (cells cannot use the insulin well). Insulin has been commercially available for the treatment of diabetes but normally in the injection forms since introduction.

Fosse Bio had collaborations with Tsinghua University for the research and development of the use of oral insulin since October, 1998. Insulin Enteric-Coated Soft Capsules, an innovative oral insulin, developed by Smart Ascent Group and Tsinghua University, have entered into Phase I/II clinical trials under the State Food and Drug Administration of the People’s Republic of China (hereinafter known as “SFDA”) and the relevant technologies have been applied for the registration of patent. As at the Valuation Date, further clinical trial of Oral Insulin has not been completed. The potential benefits of oral insulin therapy comparing with the traditional injection methods are pain-free, needle-free and it is a non-invasive drug delivery. In accordance with the market research and market estimate carried out by Fosse Bio, in 2011, there will be over 58 million diabetes patients in the People’s Republic of China (hereinafter known as the “PRC”) and it is expected that the use of oral insulin will become an alternative of injection insulin therapy in the treatment of diabetes.

As advised by Smart Ascent Group, upon passing through further clinical trial successfully and obtaining the relevant production approval, the drugs production will commence by the end of 2010.

Basis of Valuation and Assumptions

We have appraised the equity of Smart Ascent Group on the basis of “Market Value” on the premise of going concern. The going concern premise assumes that Smart Ascent Group is normally viewed as continuing in operation in the foreseeable future with neither the intention nor necessity of liquidation or of curtailing materially the scale of its operation basis. Implicit in this definition is the fact that the willing buyer would not pay more to acquire Smart Ascent Group appraised than he could reasonably expect to earn in the future from an investment in Smart Ascent Group.

The valuation of Smart Ascent Group requires consideration of all pertinent factors affecting the operations of the business and its ability to generate future investment returns. The factors considered in the appraisal including, but were not limited to, the following factors:

- the history of Smart Ascent Group;
- the economic and industry outlooks affecting Smart Ascent Group's business;
- the size and growth prospects of the Oral Insulin market in the PRC;
- the past and projected future results of Smart Ascent Group and the bases and assumptions for such results;
- the net assets and financial position of Smart Ascent Group;
- the market-derived investment returns of entities in similar line of business;
- the stage of development, timing of introduction and marketing methods for the Oral Insulin project; and
- the risks facing by Smart Ascent Group in implementing the Oral Insulin project.

The projected future results have been supplied to us by the Company. We have discussed the bases and assumptions for such results with the Directors of Smart Ascent Group and the Company. We consider such bases and assumptions are fair, reasonable and complete and have been made by the Company, whose responsibility they are, after due and careful enquiry.

In view of the ever-changing business environment in which Smart Ascent Group is operating, we have made a number of reasonable assumptions in the course of our appraisal, which are set out as follows:

- Smart Ascent Group will operate its business on continuous basis to the best of its ability and will allocate sufficient resources for the planned expansion;
- Fosse Bio will have no obstacle to obtain production approval of Oral Insulin from the SFDA after completion of the further stage of clinical trial, which is expected to take approximately 2 years;
- the financial forecasts of Smart Ascent Group are achievable;
- there will be no material changes from political, legal, economic or financial aspects in the jurisdictions in which Smart Ascent Group currently runs or intends to run its business which will materially affect its operation;
- there will be no substantial market fluctuation in the industry in the jurisdictions or states in which Smart Ascent Group currently runs or intends to run its business, which will materially affect its operations and the revenues attributed to shareholders;

- there will be no substantial fluctuation in current tax rates, interest rates and foreign currency exchange rates in the jurisdictions or states in which Smart Ascent Group currently runs or intends to run its business, which will materially affect its operations and the revenues attributed to shareholders;
- the management of Smart Ascent Group will not make any decision, which is harmful to the revenue generation ability of Smart Ascent Group's business;
- Smart Ascent Group will allocate sufficient resources to keep abreast of its future expansion; and
- the assumptions on which the financial forecasts of Smart Ascent Group will be achievable. The principal assumptions are:
 - the estimated diabetic population of the PRC in 2011 will be 58 million and is expected to grow at 0.5 million per annum to 2015;
 - operating expenses, including staff costs, administrative and marketing expenses, property related expenses, are estimated by Smart Ascent's management with reference to the scale of operations; and
 - necessary capital expenditure will be funded out of internal cash flows, plus external funding if required, and has been included in the projections as a cash outflow.

Our valuation includes a sensitivity analysis on major assumptions, particularly on the timing of commercialization of the Oral Insulin product.

In the process of valuing Smart Ascent Group, we considered the classical appraisal approaches to value, namely the Market Approach, Cost Approach and Income Approach. The Market Approach is basically a comparison method which estimates market value from analyzing sales and financial data and ratios of comparable public and, whenever possible, private companies. To the best of our understanding, there are no public sale and purchase of similar business transactions that completed in Hong Kong and the PRC. Under such circumstances, we have not relied on the Market Approach in our estimate of the Market Value of Smart Ascent Group due to insufficient supporting data.

The Cost Approach seeks to estimate the Market Value of a company by quantifying the amount of money that would be required to replace the manufacturing capabilities of the firm. In other words, this approach assumes that Smart Ascent Group's value is indicated by the cost of reproducing or replacing its manufacturing assets less an allowance for physical deterioration and obsolescence. We considered this approach is not an appropriate approach for valuing Smart Ascent Group given that the future business growth of Smart Ascent Group will be neglected.

The Income Approach focuses on the income-producing capability of a company. This approach's underlying theory is that the value of Smart Ascent Group can be measured by the present worth of the net economic benefit to be received. In our opinion, this approach is the most appropriate in valuing Smart Ascent Group since a rational buyer normally will purchase a company only if the present value of the expected economic benefits is at least equal to the purchase price. Likewise, a rational seller normally will not sell if the present value of the expected economic benefits is more than the selling

price. Thus, a sale generally will occur only at an amount equal to the economic benefits of ownership. Based on this valuation principle, we use the Income Approach to estimate the future economic benefits of Smart Ascent Group and discount these benefits to its present value using a discount rate that is appropriate for the expected risks associated with realizing those benefits.

Valuation Methodology

In choosing the Income Approach as the most appropriate method, we have used the Discounted Cash Flow (hereinafter known as “DCF”) Method, which estimates the Market Value of Smart Ascent Group by discounting the future cash flows to its present value. This would necessitate the subtraction, from the net income, the capital expenditures and changes in working capital and the addition of depreciation and amortization in the computation of cash flow. DCF analysis reflects investment criteria and requires the appraiser to make empirical and subjective assumptions.

In using the DCF Method, we adopted the Free Cash Flows to Equity (hereinafter known as “FCFE”) Technique. The FCFE Technique values the enterprise by estimating the Market Value of the ownership interests (equity) of the enterprise. This technique requires that Smart Ascent Group’s interest expenses, if any, be excluded from the free cash flows and the resulting cash flow to be discounted at the relevant rate of return required by equity. This technique then equates the value of the ownership interests as the value of the enterprise.

We derived the discount rate by using the Capital Asset Pricing Model (hereinafter known as “CAPM”). The CAPM derives the required rate of return of an asset by adding the risk-free rate to the risk premium of the asset. The CAPM is built on the premise that the variance in returns is the appropriate measure of risk but only that portion of the variance of the returns of an asset that is not reduced by diversification has to be compensated, therefore the appropriate return required of an asset is determined by the volatility of the asset’s returns relative to the returns that can be achieved by a broad market portfolio. This measured non-diversifiable risk is represented by the beta of the asset and the risk premium of the asset is its beta multiplied to the risk premium of a broad market portfolio.

In identifying the guideline companies in the relevant industries, we have referred to Standard Industrial Classification (hereinafter known as “SIC”) Code. The SIC is the statistical classification standard underlying all establishment-based Federal economic statistics classified by industry. The SIC is used to promote the comparability of establishment data describing various facets of the U.S. economy. The classification covers the entire field of economic activities and defines industries in accordance with the composition and structure of the economy.

In the course of our valuation, we used the SIC composite compound annual equity return of 10 years (SIC Code 283) from *Morningstar Inc.* as the broad market portfolio return in our CAPM computations. The category of SIC Code 283 comprises 238 companies which primarily engaged in manufacturing, fabricating, or processing medicinal chemicals and pharmaceutical products.

It is our opinion that the SIC composite compound annual equity return of 10 years represents the most reliable objective market rate of return to be used in valuing Smart Ascent Group, since it captures investors’ expectations, prevailing market conditions and the accompanying risks associated with them.

In addition to the compound annual equity return, to derive the required cost of equity in our valuation, we have added the country risk for the PRC in which Smart Ascent Group operates and business risk for its sole business operation. Majority of the guideline companies mentioned above are based and listed in the U.S., which has a more developed and liquid capital market than the PRC, thus it has the necessity to add the relevant country risk premiums to the compound annual equity return.

This study is fully cognizant of the fact that there are other relevant companies that are privately held, or are not listed in the stock exchange, or are not headquartered in the U.S.

In valuing Smart Ascent Group, we determined an unlevered Ordinary Least Squares (OLS) beta for Smart Ascent Group by deriving a representative industry beta based on a select group of companies under SIC Code 283. Some of these companies are operating the business of similar nature and have been selected as our guideline companies, which include Alkermes, Inc. (Ticker: ALKS), DepoMed Inc. (Ticker: DEPO) and Genex Biotechnology Corporation (Ticker: GNBT). These companies principally engage in the research and development of drug delivery technologies and pharmaceutical products. An unlevered beta is the beta a company would have if it had no debt. It removes a company's financial decision from the beta calculation and reflects Smart Ascent Group's business risks. The OLS betas are estimated by the traditional method of running a simple regression in which excess monthly returns on a company or composite is the dependent variable and the excess return on the market is the independent variable.

The equity risk premium of Smart Ascent Group was reached by multiplying the unlevered OLS beta to the difference between the SIC composite compound annual equity return of 10 years and the risk free rate.

The discount rate adopted in this valuation is 16.29%, which is generated by applying the risk-free rate of 3.72%, beta of 1.277, risk premium of 3.58%, country risk of 4% and business risk of 4%.

By definition, the ownership interests in closely held companies are typically not readily marketable, and by definition not as liquid and as easily converted to cash compared to similar interest in public companies. Therefore, a share of stock in a privately held company is usually worth less than an otherwise comparable share in a publicly held company. Numerous studies have been made showing that the Lack of Marketability (hereinafter known as "LOM") discount for a closely held stocks compared with a publicly traded counterpart averages between 10% and 50%, and many different researchers have obtained these averages over a wide span of years. We have opted to apply a 35% LOM discount to the value of Smart Ascent Group.

General Comments

For the purpose of this appraisal and in arriving at our opinion of value; we have relied to a very considerable extent on the information, statements, opinion and representations provided to us by Smart Ascent Group. We were furnished with the basic information of Oral Insulin and the relevant technologies, a collaboration agreement between Smart Ascent Group and Tsinghua University, a feasibility study, financial projection of Smart Ascent Group for a period of seven years ending 31 March 2015 and relevant publicly available information. These data have been utilized without further verification as correctly representing the results and future prospects of the operation and the financial condition of Smart Ascent Group.

To the best of our knowledge, all data set forth in this report are true and accurate. Although gathered from reliable sources, no guarantee is made nor liability assumed for the accuracy of any data, opinions, or estimates identified as being furnished by others, which have been used in formulating this analysis.

We are unable to accept any responsibilities for the operation and financial information that have not been supplied to us by Smart Ascent Group and the Company. We have had no reason to doubt the authenticity and accuracy of the information provided or the reasonableness of the opinions expressed by Smart Ascent Group, the Company and their directors, which have been provided to us. We also sought and received confirmation that no material factors have been omitted from the information provided.

In the course of our valuation, we relied on Smart Ascent Group's financial projections during the 7 years' forecast period. We have tested this estimate against relevant data pertaining to the various economies and the replication industry, and find it is fair and reasonable.

In arriving at our opinion, we have assumed that Smart Ascent Group has adopted necessary security measures and has considered several contingency plans to protect and maintain the reliability of its business.

We have assumed that the appraised equity of Smart Ascent Group is freely disposable and transferable for its existing or alternative uses in the open market disregarding any further tax, fee and charges payable to the government upon disposal.

In the course of our valuation, we have adopted the basis of valuation and made the valuation assumptions in accordance with the International Valuation Standards (Eight Edition) published by The International Valuation Standards Committee and The HKIS Valuation Standards on Trade-Related Business Assets and Business Enterprises (First Edition, 2004) published by the Hong Kong Institute of Surveyors.

We have made no investigation of the legal title or any liabilities attached to Smart Ascent Group. All legal documents disclosed (if any) are for reference only and no responsibility is assumed for any legal matters concerning the legal title and the rights (if any) to Smart Ascent Group. We have not verified the original documents furnished to us, any responsibility for our misinterpretation of the legal documents, therefore, cannot be accepted. Besides, we are not in a position to advise and comment on the title and encumbrances to Smart Ascent Group.

No allowance has been made in our valuation for any charges or amounts owing neither on Smart Ascent Group nor for any expenses or taxation, which may be incurred in effecting a sale. It is assumed that Smart Ascent Group will be rendered free from encumbrances, restrictions and outgoings of any onerous nature, which could affect its value.

Unless otherwise stated, the base currency of this report is Hong Kong Dollar.

Opinion of Value

Based on the analysis, reasoning and data outlined as above, and on the appraisal method employed, it is our opinion that as at the Valuation Date, the Market Value of Smart Ascent Group (100% equity interest of Smart Ascent, which owns as to 51% equity interest of Fosse Bio and 51% equity interest of Welly Surplus) is reasonably stated by the amount of **HK\$1,547,241,000 (HONG KONG DOLLARS ONE BILLION FIVE HUNDRED FORTY-SEVEN MILLION TWO HUNDRED AND FORTY-ONE THOUSAND ONLY)**.

A sensitivity analysis has been made on the assumption that the discount rate has a fluctuation of $\pm 1\%$. The result of the sensitivity analysis is set out as follows:

Discount Rate	Valuation Result <i>HK\$'000</i>	Difference <i>HK\$'000</i>
17.29%	1,411,532	(135,709)
16.29%	1,547,241	—
15.29%	1,704,937	157,696

The conclusion of value is based on generally accepted appraisal procedures and practices that rely extensively on assumptions and considerations, not all of which can be easily quantified or ascertained exactly. While we have exercised our professional judgment in arriving at the appraisal, you are urged to consider carefully the nature of such assumptions, which are disclosed in this report and should exercise caution when interpreting this report.

We hereby certify that we have neither present nor prospective interest in Smart Ascent Group nor the Company or the value reported.

Yours faithfully,

For and on behalf of

Castores Magi Asia Limited

Deret Au Chi Chung

*Member of China Institute of Real Estate Appraisers and Agents
Registered Business Valuer of Hong Kong Business Valuation Forum
B.Sc. MRICS MHKIS RPS MCIArb AHKIArb*

Director

2. LETTER FROM THE REPORTING ACCOUNTANTS ON THE ACCOUNTING POLICIES AND CALCULATION FOR THE VALUATION

The following is the text of the report dated 21 May 2009 from the reporting accountants, RSM Nelson Wheeler in connection with the valuation of the Smart Ascent Group as at 28 February 2009, prepared for the purpose of incorporation in this circular.

RSM Nelson Wheeler
中瑞岳華(香港)會計師事務所
Certified Public Accountants

29th Floor
Caroline Centre
Lee Gardens Two
28 Yun Ping Road
Hong Kong

21 May 2009

The Board of Directors
Extrawell Pharmaceutical Holdings Limited

Dear Sirs,

We have examined the principal accounting policies adopted in and the arithmetical accuracy of the calculations of the discounted cash flow forecast (the “Forecast”) underlying the valuation (the “Valuation”) of Smart Ascent Limited and its subsidiaries (the “Smart Ascent Group”) performed by Castores Magi Asia Limited (the “Valuer”) in respect of the appraisal of the fair value of the Smart Ascent Group as at the reference date of 28 February 2009 in connection with the circular of Extrawell Pharmaceutical Holdings Limited (the “Company”) dated 21 May 2009 (the “Circular”).

Respective responsibilities of directors and RSM Nelson Wheeler

The directors of the Company are responsible for the preparation of the Forecast and the reasonableness and validity of the assumptions based on which the Forecast is prepared (the “Assumptions”).

It is our responsibility to form an opinion based on our reasonable assurance engagement, so far as the accounting policies and the arithmetical accuracy of the calculations are concerned, on whether the Forecast has been properly compiled, in all material respects, in accordance with the Assumptions and on a basis consistent with the accounting policies normally adopted by the Company as set out in the audited consolidated financial statements of the Company for the year ended 31 March 2008 and to report our opinion solely to you, as a body, solely for the purpose in connection with the Circular and for no other purpose. We accept no responsibility to any other person in respect of, arising out of, or in connection with our work.

The Assumptions include hypothetical assumptions about future events and management actions that may or may not necessarily be expected to occur. Even if the events and actions anticipated do occur, actual results are still likely to be different from the Forecast and the variation may be material. Accordingly we have not reviewed, considered or conducted any work on the reasonableness and the validity of the Assumptions and do not express opinion whatsoever thereon.

Basis of opinion

We conducted our reasonable assurance engagement in accordance with Hong Kong Standard on Assurance Engagements 3000 “Assurance Engagements Other Than Audits or Reviews of Historical Financial Information” with reference to the procedures under Auditing Guideline 3.341 “Accountants’ Report on Profit Forecasts” issued by the Hong Kong Institute of Certified Public Accountants (the “HKICPA”). Our work was performed solely to assist the directors of the Company to evaluate, so far as the accounting policies and the arithmetical accuracy of the calculations are concerned, whether the Forecast has been properly compiled, in all material respects, in accordance with the Assumptions and on a basis consistent with the accounting policies normally adopted by the Company as set out in the audited consolidated financial statements of the Company for the year ended 31 March 2008.

We planned and performed our reasonable assurance engagement so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to give our opinion. Our reasonable assurance engagement included:

- a. obtaining an understanding of the principal accounting policies adopted in the preparation of the Forecast through inquiry of persons responsible for financial and accounting matters;
- b. comparing the principal accounting policies adopted in the preparation of the Forecast with those adopted in the preparation of the audited consolidated financial statements of the Company for the year ended 31 March 2008; and
- c. checking the arithmetical calculations relating to the amounts presented in the Forecast.

We believe that our reasonable assurance engagement provides a reasonable basis for our opinion.

Our reasonable assurance engagement does not constitute an audit or a review conducted in accordance with Hong Kong Standards on Auditing or Hong Kong Standards on Review Engagements issued by the HKICPA. Accordingly, we do not express an audit or a review opinion on the Forecast.

Opinion

In our opinion, based on the foregoing, so far as the accounting policies and the arithmetical accuracy of the calculations are concerned, the Forecast has been properly compiled, in all material respects, in accordance with the Assumptions and on a basis consistent with the accounting policies normally adopted by the Company as set out in the audited consolidated financial statements of the Company for the year ended 31 March 2008.

Yours faithfully,
RSM Nelson Wheeler
Certified Public Accountants
Hong Kong

The following is the text of a report, prepared for the sole purpose of inclusion in this circular, from the independent reporting accountants, RSM Nelson Wheeler, Certified Public Accountants, Hong Kong.

RSM Nelson Wheeler
 中瑞岳華(香港)會計師事務所
 Certified Public Accountants

29th Floor
 Caroline Centre
 Lee Gardens Two
 28 Yun Ping Road
 Hong Kong

21 May 2009

The Board of Directors
 Extrawell Pharmaceutical Holdings Limited

Dear Sirs,

We set out below our report on the financial information (the “Financial Information”) of Smart Ascent Limited (“Smart Ascent”) and its subsidiaries (hereinafter collectively referred to as “Smart Ascent Group”) for each of the three years ended 31 March 2006, 2007 and 2008 and the five months ended 31 August 2007 and 2008 (the “Relevant Periods”) for inclusion in the circular dated 21 May 2009 (the “Circular”) issued by Extrawell Pharmaceutical Holdings Limited (the “Company”) in connection with the Company’s acquisition of the 51% equity interest in Smart Ascent.

Smart Ascent was incorporated on 1 December 2000 in Hong Kong with limited liability and acts as an investment holding company. As at the date of this report, Smart Ascent has direct interests in the following subsidiaries:

Name	Place and date of incorporation and operation	Issued and paid up capital	Percentage of equity interest	Principal activities
Fosse Bio-Engineering Development Limited (“Fosse Bio”)	Hong Kong 28 September 1998	10,000 ordinary shares of HK\$10 each	51%	Research and development and commercialisation of oral insulin products
Welly Surplus Development Limited (“Welly Surplus”)	Hong Kong 6 August 2004	100 ordinary shares of HK\$1 each	51%	Inactive

Smart Ascent adopts 31 March as its financial year end date.

No audited financial statements have been prepared for Fosse Bio and Welly Surplus for the Relevant Periods.

Statutory financial statements of Smart Ascent for the year ended 31 March 2006 were audited by HLB Hodgson Impey Cheng, certified public accountants registered in Hong Kong. No statutory audited financial statements of Smart Ascent have been prepared for the year ended 31 March 2007. We have audited the statutory financial statements of Smart Ascent for the year ended 31 March 2008.

For the purpose of this report, the directors of Smart Ascent have prepared the consolidated financial statements of Smart Ascent and its subsidiaries for the Relevant Periods (the “HKFRS Financial Statements”) in accordance with Hong Kong Financial Reporting Standards (“HKFRS”) issued by the Hong Kong Institute of Certified Public Accountants (the “HKICPA”).

We have performed our independent audit on the HKFRS Financial Statements in accordance with Hong Kong Standards on Auditing issued by the HKICPA and have examined the HKFRS Financial Statements in accordance with Auditing Guideline 3.340 “Prospectuses and the Reporting Accountant” issued by the HKICPA.

The Financial Information has been prepared from the HKFRS Financial Statements in accordance with HKFRSs. No adjustments were considered necessary for the purpose of preparing our report for inclusion in the Circular.

The directors of Smart Ascent are responsible for the preparation of the HKFRS Financial Statements which give a true and fair view. In preparing the HKFRS Financial Statements, it is fundamental that appropriate accounting policies are selected and applied consistently. The directors of the Company are responsible for the contents of the Circular in which this report is included. It is our responsibility to compile the Financial Information set out in this report from the HKFRS Financial Statements, to form an independent opinion on the Financial Information and to report our opinion to you.

Basis for disclaimer of opinion

- (a) As set out in note 10 to the Financial Information, included in the intangible assets as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008 is the technological know-how with carrying value of HK\$281,473,437 (“Know-how”) in relation to an oral insulin product (the “Product”) and the exclusive right for the commercialisation of the Product owned by Smart Ascent Group. The Know-how is held by Fosse Bio, a subsidiary acquired by Smart Ascent during the year ended 31 March 2004. In addition, as set out in note 12 to the Financial Information, included in other receivables as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008 is a receivable with carrying amount of HK\$31,780,000 (the “Receivable”) owed by Mr. Ong Cheng Heang and Ms. Wu Kiet Ming (the “Vendors”) to Smart Ascent Group. The Receivable is secured on the remaining 49% equity interest in Smart Ascent held by Mr. Ong Cheng Heang. As further set out in notes 10 and 12, the recoverability of the carrying values of the Know-how and the Receivable depends upon the result of the clinical trials and the successful launching of the Product, the outcome of which is currently uncertain. The Financial Information does not include any adjustments that may be necessary should the clinical trials or the launching of the Product be unsuccessful. We consider that the significant uncertainty has been adequately disclosed in the Financial Information. However, in view of the extent of the significant uncertainty, we disclaim our opinion in respect of the carrying values of the Know-how and the Receivable as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008.

Any adjustments to the above figures might have a significant consequential effect on Smart Ascent Group’s results for the Relevant Periods and net assets of Smart Ascent Group as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008.

- (b) We have not been provided with sufficient evidence to satisfy ourselves as to the recoverability of Smart Ascent's investments in subsidiaries of HK\$40,065,711 as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008 and the total amount of HK\$2,530,189 due from subsidiaries as at 31 March 2006 and the total amount of HK\$3,446,488 due from subsidiaries as at 31 March 2007 and 2008, and 31 August 2007 and 2008. Consequently we are unable to determine whether any provision for impairment should be made.

Any adjustments to the above figures might have a significant consequential effect on the net assets of Smart Ascent as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008.

Disclaimer of opinion: disclaimer on view given by the Financial Information

Because of the significance of the matters described in the basis for disclaimer of opinion paragraphs, we do not express an opinion on the Financial Information as to whether the Financial Information gives a true and fair view of the state of the affairs of Smart Ascent and of Smart Ascent Group as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008 and of Smart Ascent Group's results and cash flows for the Relevant Periods in accordance with Hong Kong Financial Reporting Standards.

Material uncertainty relating to the going concern basis

Without qualifying our opinion, we draw attention to note 2 to the Financial Information which mentions that Smart Ascent Group incurred a loss attributable to the equity holders of Smart Ascent of HK\$158,819 for the five months ended 31 August 2008 and as at 31 August 2008 Smart Ascent Group had net current liabilities of HK\$3,717,928. These conditions indicate the existence of a material uncertainty which may cast significant doubt about Smart Ascent Group's ability to continue as a going concern. The Financial Information has been prepared on a going concern basis, the validity of which depends upon the financial support from the ultimate parent at a level sufficient to finance the working capital requirements of Smart Ascent Group to meet its liabilities as they fall due. The Financial Information does not include any adjustments that would result from the failure to obtain the financial support. We consider that the material uncertainty has been adequately disclosed in the Financial Information.

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

I. FINANCIAL INFORMATION

Consolidated Income Statements

	<i>Note</i>	For the year ended 31 March			For the five months ended 31 August	
		2006 <i>HK\$</i>	2007 <i>HK\$</i>	2008 <i>HK\$</i>	2007 <i>HK\$</i>	2008 <i>HK\$</i>
Turnover	7	—	—	—	—	—
Administrative expenses		(278,381)	(215,481)	(502,322)	(90,832)	(158,819)
Loss before tax		(278,381)	(215,481)	(502,322)	(90,832)	(158,819)
Income tax expense	8	—	—	—	—	—
Loss for the year/period	9	(278,381)	(215,481)	(502,322)	(90,832)	(158,819)
Attributable to:						
Equity holders of Smart Ascent		(266,978)	(197,703)	(475,303)	(90,832)	(158,819)
Minority interests		(11,403)	(17,778)	(27,019)	—	—
		(278,381)	(215,481)	(502,322)	(90,832)	(158,819)

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

Consolidated Balance Sheets

		As at 31 March			As at 31 August	
		2006	2007	2008	2007	2008
	Note	HK\$	HK\$	HK\$	HK\$	HK\$
Non-current assets						
Intangible assets	10	281,473,437	281,473,437	281,473,437	281,473,437	281,473,437
Current assets						
Other receivables	12	32,607,551	33,503,702	33,503,702	33,503,702	33,503,702
Bank and cash balances		8,913	4,353	1,377	4,003	2,527
		<u>32,616,464</u>	<u>33,508,055</u>	<u>33,505,079</u>	<u>33,507,705</u>	<u>33,506,229</u>
Current liabilities						
Accruals and other payables		238,127	203,309	560,657	241,393	389,987
Due to the immediate holding company	13	2,815,751	3,957,641	4,099,639	4,010,039	4,430,278
Due to a minority shareholder	13	<u>32,403,892</u>	<u>32,403,892</u>	<u>32,403,892</u>	<u>32,403,892</u>	<u>32,403,892</u>
		<u>35,457,770</u>	<u>36,564,842</u>	<u>37,064,188</u>	<u>36,655,324</u>	<u>37,224,157</u>
Net current liabilities		<u>(2,841,306)</u>	<u>(3,056,787)</u>	<u>(3,559,109)</u>	<u>(3,147,619)</u>	<u>(3,717,928)</u>
NET ASSETS		<u>278,632,131</u>	<u>278,416,650</u>	<u>277,914,328</u>	<u>278,325,818</u>	<u>277,755,509</u>
Capital and reserves						
Share capital	14	10,000	10,000	10,000	10,000	10,000
Reserves	15(a)	<u>141,881,441</u>	<u>141,683,738</u>	<u>141,208,435</u>	<u>141,592,906</u>	<u>141,049,616</u>
Equity attributable to equity holders of Smart Ascent		141,891,441	141,693,738	141,218,435	141,602,906	141,059,616
Minority interests		<u>136,740,690</u>	<u>136,722,912</u>	<u>136,695,893</u>	<u>136,722,912</u>	<u>136,695,893</u>
TOTAL EQUITY		<u>278,632,131</u>	<u>278,416,650</u>	<u>277,914,328</u>	<u>278,325,818</u>	<u>277,755,509</u>

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

Balance Sheets — Smart Ascent

		As at 31 March			As at 31 August	
		2006	2007	2008	2007	2008
	Note	HK\$	HK\$	HK\$	HK\$	HK\$
Non-current assets						
Investments in subsidiaries	11	40,065,711	40,065,711	40,065,711	40,065,711	40,065,711
Current assets						
Other receivables	12	31,780,000	31,780,000	31,780,000	31,780,000	31,780,000
Due from subsidiaries	13	2,530,189	3,446,488	3,446,488	3,446,488	3,446,488
Bank and cash balances		6,420	3,370	1,270	3,020	2,420
		<u>34,316,609</u>	<u>35,229,858</u>	<u>35,227,758</u>	<u>35,229,508</u>	<u>35,228,908</u>
Current liabilities						
Other payables		151,308	101,916	405,000	140,000	234,330
Due to a subsidiary	13	51	—	—	—	—
Due to the immediate holding company	13	2,815,751	3,957,641	4,099,639	4,010,039	4,430,278
Due to a minority shareholder	13	<u>31,780,000</u>	<u>31,780,000</u>	<u>31,780,000</u>	<u>31,780,000</u>	<u>31,780,000</u>
		<u>34,747,110</u>	<u>35,839,557</u>	<u>36,284,639</u>	<u>35,930,039</u>	<u>36,444,608</u>
Net current liabilities		<u>(430,501)</u>	<u>(609,699)</u>	<u>(1,056,881)</u>	<u>(700,531)</u>	<u>(1,215,700)</u>
NET ASSETS		<u>39,635,210</u>	<u>39,456,012</u>	<u>39,008,830</u>	<u>39,365,180</u>	<u>38,850,011</u>
Capital and reserves						
Share capital	14	10,000	10,000	10,000	10,000	10,000
Reserves	15(b)	<u>39,625,210</u>	<u>39,446,012</u>	<u>38,998,830</u>	<u>39,355,180</u>	<u>38,840,011</u>
TOTAL EQUITY		<u>39,635,210</u>	<u>39,456,012</u>	<u>39,008,830</u>	<u>39,365,180</u>	<u>38,850,011</u>

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

Consolidated Statements of Changes in Equity

	Attributable to equity holders of Smart Ascent			Minority interests HK\$	Total HK\$
	Share capital HK\$	Retained profits HK\$	Total HK\$		
At 1 April 2005	10,000	142,148,419	142,158,419	136,771,299	278,929,718
Acquisition of a subsidiary	—	—	—	(19,206)	(19,206)
Loss for the year	—	(266,978)	(266,978)	(11,403)	(278,381)
At 31 March 2006 and 1 April 2006	10,000	141,881,441	141,891,441	136,740,690	278,632,131
Loss for the year	—	(197,703)	(197,703)	(17,778)	(215,481)
At 31 March 2007 and 1 April 2007	10,000	141,683,738	141,693,738	136,722,912	278,416,650
Loss for the year	—	(475,303)	(475,303)	(27,019)	(502,322)
At 31 March 2008 and 1 April 2008	10,000	141,208,435	141,218,435	136,695,893	277,914,328
Loss for the period	—	(158,819)	(158,819)	—	(158,819)
At 31 August 2008	<u>10,000</u>	<u>141,049,616</u>	<u>141,059,616</u>	<u>136,695,893</u>	<u>277,755,509</u>
At 1 April 2007	10,000	141,683,738	141,693,738	136,722,912	278,416,650
Loss for the period	—	(90,832)	(90,832)	—	(90,832)
At 31 August 2007	<u>10,000</u>	<u>141,592,906</u>	<u>141,602,906</u>	<u>136,722,912</u>	<u>278,325,818</u>

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

Consolidated Cash Flow Statements

		For the year ended 31 March			For the five months ended 31 August	
		2006	2007	2008	2007	2008
	Note	HK\$	HK\$	HK\$	HK\$	HK\$
CASH FLOWS FROM OPERATING ACTIVITIES						
Loss before tax		(278,381)	(215,481)	(502,322)	(90,832)	(158,819)
Adjustment for:						
Impairment of goodwill		20,039	—	—	—	—
Operating loss before working capital charges		(258,342)	(215,481)	(502,322)	(90,832)	(158,819)
Increase in other receivables		(814,090)	(896,151)	—	—	—
(Decrease)/Increase in accruals and other payables		(534,168)	(34,818)	357,348	38,084	(170,670)
Increase in amount due to the immediate holding company		1,585,562	1,141,890	141,998	52,398	330,639
Net cash (used in)/generated from operating activities		(21,038)	(4,560)	(2,976)	(350)	1,150
CASH FLOWS FROM INVESTING ACTIVITIES						
Acquisition of a subsidiary	16	706	—	—	—	—
Net cash generated from investing activities		706	—	—	—	—
NET (DECREASE)/ INCREASE IN CASH AND CASH EQUIVALENTS						
		(20,332)	(4,560)	(2,976)	(350)	1,150
CASH AND CASH EQUIVALENTS AT BEGINNING OF YEAR/ PERIOD						
		29,245	8,913	4,353	4,353	1,377
CASH AND CASH EQUIVALENTS AT END OF YEAR/PERIOD						
		8,913	4,353	1,377	4,003	2,527
ANALYSIS OF CASH AND CASH EQUIVALENTS						
Bank and cash balances		8,913	4,353	1,377	4,003	2,527

II. NOTES TO THE FINANCIAL INFORMATION

1. GENERAL INFORMATION

Smart Ascent was incorporated in Hong Kong with limited liability under the Hong Kong Companies Ordinance. The address of its registered office and its principal place of business is Room 3409-10, 34/F., China Resources Building, 26 Harbour Road, Wanchai, Hong Kong.

Smart Ascent is an investment holding company. The principal activities of its subsidiaries are set in note 11 to the Financial Information.

In the opinion of the directors of Smart Ascent, Extrawell (BVI) Limited, a company incorporated in the British Virgin Islands, is the immediate parent, and Extrawell Pharmaceutical Holdings Limited, a company incorporated in Bermuda, is the ultimate parent of Smart Ascent.

2. GOING CONCERN BASIS

Smart Ascent Group incurred a loss attributable to equity holders of Smart Ascent of HK\$158,819 for the five months ended 31 August 2008 and as at 31 August 2008 Smart Ascent Group had net current liabilities of HK\$3,717,928. These conditions indicate the existence of a material uncertainty which may cast significant doubt on Smart Ascent Group's ability to continue as a going concern. Therefore, Smart Ascent Group may be unable to realise its assets and discharge its liabilities in the normal course of business.

The Financial Information has been prepared on a going concern basis, the validity of which depends upon the financial support from the ultimate parent at a level sufficient to finance the working capital requirements of Smart Ascent Group to meet its liabilities as they fall due. The ultimate parent has agreed to provide adequate funds for Smart Ascent to meet its liabilities as they fall due. The directors of Smart Ascent are therefore of the opinion that it is appropriate to prepare the Financial Information on a going concern basis. Should Smart Ascent Group be unable to continue as a going concern, adjustments would have to be made to the Financial Information to adjust the value of Smart Ascent Group's assets to their recoverable amounts, to provide for any further liabilities which might arise and to reclassify non-current assets as current assets.

3. ADOPTION OF NEW AND REVISED HONG KONG FINANCIAL REPORTING STANDARDS

During the Relevant Periods, Smart Ascent Group has adopted all the new and revised HKFRSs that are relevant to its operations and effective for its accounting period beginning on 1 April 2008. HKFRSs comprise Hong Kong Financial Reporting Standards; Hong Kong Accounting Standards; and Interpretations.

Smart Ascent Group has not applied the new HKFRSs that have been issued but are not yet effective. Smart Ascent Group has already commenced an assessment of the impact of these new HKFRSs but is not yet in a position to state whether these new HKFRSs would have a material impact on its results of operation and financial position.

4. SIGNIFICANT ACCOUNTING POLICIES

The Financial Information has been prepared in accordance with HKFRSs, accounting principles generally accepted in Hong Kong and the applicable disclosures required by the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited and the Hong Kong Companies Ordinance.

The Financial Information has been prepared under the historical cost convention.

The preparation of Financial Information in conformity with HKFRSs requires the use of certain key assumptions and estimates. It also requires the directors to exercise its judgements in the process of applying the accounting policies. The areas involving critical judgements and areas where assumptions and estimates are significant to the Financial Information, are disclosed in note 5 to the Financial Information.

The significant accounting policies applied in the preparation of the Financial Information are set out below.

(a) Consolidation

The Financial Information includes the financial statements of Smart Ascent and its subsidiaries made up to 31 March. Subsidiaries are entity over which Smart Ascent Group has control. Control is the power to govern the financial and operating policies of an entity so as to obtain benefits from its activities. The existence and effect of potential voting rights that are currently exercisable or convertible are considered when assessing whether Smart Ascent Group has control.

Subsidiaries are fully consolidated from the date on which control is transferred to Smart Ascent Group. They are de-consolidated from the date the control ceases.

The gain or loss on the disposal of a subsidiary represents the difference between the proceeds of the sale of Smart Ascent Group's share of its net assets together with any goodwill relating to the subsidiary which was not previously charged or recognised in the consolidated income statement and also any related accumulated foreign currency translation reserve.

Inter-company transactions, balances and unrealised profits on transactions between Smart Ascent Group companies are eliminated. Unrealised losses are also eliminated unless the transaction provides evidence of an impairment of the asset transferred. Accounting policies of subsidiaries have been changed where necessary to ensure consistency with the policies adopted by Smart Ascent Group.

Minority interests represent the interests of minority shareholders in the operating results and net assets of subsidiaries. Minority interests are presented in the consolidated balance sheet and consolidated statement of changes in equity within equity. Minority interests are presented in the consolidated income statement as an allocation of profit or loss for the year between minority and shareholders of Smart Ascent. Losses applicable to the minority in excess of the minority's interests in the subsidiary's equity are allocated against the interests of Smart Ascent Group except to the extent that the minority has a binding obligation and is able to make an additional investment to cover the losses. If the subsidiary subsequently reports profits, such profits are allocated to the interests of Smart Ascent Group until the minority's share of losses previously absorbed by Smart Ascent Group has been recovered.

In Smart Ascent's balance sheet the investments in subsidiaries are stated at cost less allowance for impairment losses. The results of subsidiaries are accounted for by Smart Ascent on the basis of dividends received and receivable.

(b) Business combination and goodwill

The purchase method of accounting is used to account for the acquisition of subsidiaries by Smart Ascent Group. The cost of an acquisition is measured as the fair value of the assets given, equity instruments issued and liabilities incurred or assumed at the date of exchange, plus costs directly attributable to the acquisition. Identifiable assets, liabilities and contingent liabilities of the subsidiary in an acquisition are measured at their fair values at the acquisition date.

The excess of the cost of acquisition over Smart Ascent Group's share of the net fair value of the subsidiary's identifiable assets, liabilities and contingent liabilities is recorded as goodwill. Any excess of Smart Ascent Group's share of the net fair value of the identifiable assets, liabilities and contingent liabilities over the cost of acquisition is recognised in the consolidated income statement.

Goodwill is tested annually for impairment and carried at cost less accumulated impairment losses. Impairment losses of goodwill are recognised in the consolidated income statement and are not subsequently reversed. Goodwill is allocated to cash-generating units for the purpose of impairment testing.

The interests of minority shareholders in the subsidiary is initially measured at the minority's proportion of the net fair value of the subsidiary's identifiable assets, liabilities and contingent liabilities at the acquisition date.

(c) Foreign currency translation

(i) Functional and presentation currency

Items included in the financial statements of each of Smart Ascent Group's entities are measured using the currency of the primary economic environment in which the entity operates (the "functional currency"). The Financial Information is presented in Hong Kong dollars ("HK\$"), which is Smart Ascent's functional and presentation currency.

(ii) Transactions and balances in each entity's financial statements

Transactions in foreign currencies are translated into the functional currency using the exchange rates prevailing on the transaction dates. Monetary assets and liabilities in foreign currencies are translated at the rates ruling on the balance sheet date. Profits and losses resulting from this translation policy are included in the income statement.

(iii) Translation on consolidation

The results and financial position of all Smart Ascent Group entities that have a functional currency different from Smart Ascent's presentation currency are translated into Smart Ascent's presentation currency as follows:

- Assets and liabilities for each balance sheet presented are translated at the closing rate at the date of that balance sheet;
- Income and expenses for each income statement are translated at average exchange rates (unless this average is not a reasonable approximation of the cumulative effect of the rates prevailing on the transaction dates, in which case income and expenses are translated at the exchange rates on the transaction dates); and
- All resulting exchange differences are recognised in the foreign currency translation reserve.

On consolidation, exchange differences arising from the translation of the net investment in foreign entities and of borrowings are recognised in the foreign currency translation reserve. When a foreign operation is sold, such exchange differences are recognised in the consolidated income statement as part of the profit or loss on disposal.

Goodwill and fair value adjustments arising on the acquisition of a foreign entity are treated as assets and liabilities of the foreign entity and translated at the closing rate.

(d) Research and development expenditure

Expenditure on research activities is recognised as an expense in the period in which it is incurred. An internally generated intangible asset arising from Smart Ascent Group's products development is recognised only if all of the following conditions are met:

- An asset is created that can be identified (such as software and new processes);
- It is probable that the asset created will generate future economic benefits; and
- The development cost of the asset can be measured reliably.

(e) Intangible assets

Technological know-how represents the rights for development and commercialisation of an oral insulin product.

Technological know-how is not amortised as the rights are not yet available for use.

(f) Recognition and derecognition of financial instruments

Financial assets and financial liabilities are recognised in the balance sheet when Smart Ascent Group becomes a party to the contractual provisions of the instruments.

Financial assets are derecognised when the contractual rights to receive cash flows from the assets expire; Smart Ascent Group transfers substantially all the risks and rewards of ownership of the assets; or Smart Ascent Group neither transfers nor retains substantially all the risks and rewards of ownership of the assets but has not retained control on the assets. On derecognition of a financial asset, the difference between the asset's carrying amount and the sum of the consideration received and receivable and the cumulative gain or loss that had been recognised directly in equity is recognised in the income statement.

Financial liabilities are derecognised when the obligation specified in the relevant contract is discharged, cancelled or expires. The difference between the carrying amount of the financial liability derecognised and the consideration paid is recognised in the income statement.

(g) Other receivables

Other receivables are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market and are recognised initially at fair value and subsequently measured at amortised cost using the effective interest method, less allowance for impairment. An allowance for impairment of other receivables is established when there is objective evidence that Smart Ascent Group will not be able to collect all amounts due according to the original terms of receivables. The amount of the allowance is the difference between the receivables' carrying amount and the present value of estimated future cash flows, discounted at the effective interest rate computed at initial recognition. The amount of the allowance is recognised in the income statement.

Impairment losses are reversed in subsequent periods and recognised in the income statement when an increase in the receivables' recoverable amount can be related objectively to an event occurring after the impairment was recognised, subject to the restriction that the carrying amount of the receivables at the date the impairment is reversed shall not exceed what the amortised cost would have been had the impairment not been recognised.

(h) Cash and cash equivalents

For the purpose of the cash flow statement, cash and cash equivalents represent cash at bank and on hand, demand deposits with banks and other financial institutions, and short-term highly liquid investments which are readily convertible into known amounts of cash and subject to an insignificant risk of change in value. Bank overdrafts which are repayable on demand and form an integral part of Smart Ascent Group's cash management are also included as a component of cash and cash equivalents.

(i) Financial liabilities and equity instruments

Financial liabilities and equity instruments are classified according to the substance of the contractual arrangements entered into and the definitions of a financial liability and an equity instrument under HKFRSs. An equity instrument is any contract that evidences a residual interest in the assets of Smart Ascent Group after deducting all of its liabilities. The accounting policies adopted for specific financial liabilities and equity instruments are set out below:

(i) Other payables

Other payables are stated initially at their fair value and subsequently measured at amortised cost using the effective interest method unless the effect of discounting would be immaterial, in which case they are stated at cost.

(ii) Equity instruments

Equity instruments issued by Smart Ascent are recorded at the proceeds received, net of direct issue costs.

(j) Taxation

Income tax represents the sum of the current tax and deferred tax.

The tax currently payable is based on taxable profit for the year. Taxable profit differs from profit as reported in the income statement because it excludes items of income or expense that are taxable or deductible in other years and it further excludes items that are never taxable or deductible. Smart Ascent Group's liability for current tax is calculated using tax rates that have been enacted or substantively enacted by the balance sheet date.

Deferred tax is recognised on differences between the carrying amounts of assets and liabilities in the Financial Information and the corresponding tax bases used in the computation of taxable profit, and is accounted for using the balance sheet liability method. Deferred tax liabilities are generally recognised for all taxable temporary differences and deferred tax assets are recognised to the extent that it is probable that taxable profits will be available against which deductible temporary differences, unused tax losses or unused tax credits can be utilised. Such assets and liabilities are not recognised if the temporary difference arises from goodwill or from the initial recognition (other than in a business combination) of other assets and liabilities in a transaction that affects neither the taxable profit nor the accounting profit.

Deferred tax liabilities are recognised for taxable temporary differences arising on investments in subsidiaries except where Smart Ascent Group is able to control the reversal of the temporary difference and it is probable that the temporary difference will not reverse in the foreseeable future.

The carrying amount of deferred tax assets is reviewed at each balance sheet date and reduced to the extent that it is no longer probable that sufficient taxable profits will be available to allow all or part of the asset to be recovered.

Deferred tax is calculated at the tax rates that are expected to apply in the period when the liability is settled or the asset is realised, based on tax rates that have been enacted or substantively enacted by the balance sheet date. Deferred tax is charged or credited to the income statement, except when it relates to items charged or credited directly to equity, in which case the deferred tax is also dealt with in equity.

Deferred tax assets and liabilities are offset when there is a legally enforceable right to set off current tax assets against current tax liabilities and when they relate to income taxes levied by the same taxation authority and Smart Ascent Group intends to settle its current tax assets and liabilities on a net basis.

(k) Related parties

A party is related to Smart Ascent Group if:

- (i) directly or indirectly through one or more intermediaries, the party controls, is controlled by, or is under common control with, Smart Ascent Group; has an interest in Smart Ascent Group that gives it significant influence over Smart Ascent Group; or has joint control over Smart Ascent Group;
- (ii) the party is an associate;
- (iii) the party is a joint venture;
- (iv) the party is a member of the key management personnel of Smart Ascent or its parent;
- (v) the party is a close member of the family of any individual referred to in (i) or (iv);
- (vi) the party is an entity that is controlled, jointly controlled or significantly influenced by or for which significant voting power in such entity resides with, directly or indirectly, any individual referred to in (iv) or (v); or
- (vii) the party is a post-employment benefit plan for the benefit of employees of Smart Ascent Group, or of any entity that is a related party of Smart Ascent Group.

(l) Impairment of assets

Intangible assets that have an indefinite useful life or not yet available for use are reviewed annually for impairment and are reviewed for impairment whenever events or changes in circumstances indicate the carrying amount may not be recoverable.

At each balance sheet date, Smart Ascent Group reviews the carrying amounts of its tangible and other intangible assets except receivables to determine whether there is any indication that those assets have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of any impairment loss. Where it is not possible to estimate the recoverable amount of an individual asset, Smart Ascent Group estimates the recoverable amount of the cash-generating unit to which the asset belongs.

Recoverable amount is the higher of fair value less costs to sell and value in use. In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset.

If the recoverable amount of an asset or cash-generating unit is estimated to be less than its carrying amount, the carrying amount of the asset or cash-generating unit is reduced to its recoverable amount. An impairment loss is recognised immediately in the income statement, unless the relevant asset is carried at a revalued amount, in which case the impairment loss is treated as a revaluation decrease.

Where an impairment loss subsequently reverses, the carrying amount of the asset or cash-generating unit is increased to the revised estimate of its recoverable amount, but so that the increased carrying amount does not exceed the carrying amount that would have been determined (net of amortisation or depreciation) had no impairment loss been recognised for the asset or cash-generating unit in prior years. A reversal of an impairment loss is recognised immediately in the income statement, unless the relevant asset is carried at a revalued amount, in which case the reversal of the impairment loss is treated as a revaluation increase.

(m) Provisions and contingent liabilities

Provisions are recognised for liabilities of uncertain timing or amount when Smart Ascent Group has a present legal or constructive obligation arising as a result of a past event, it is probable that an outflow of economic benefits will be required to settle the obligation and a reliable estimate can be made. Where the time value of money is material, provisions are stated at the present value of the expenditures expected to settle the obligation.

Where it is not probable that an outflow of economic benefits will be required, or the amount cannot be estimated reliably, the obligation is disclosed as a contingent liability, unless the probability of outflow is remote. Possible obligations, whose existence will only be confirmed by the occurrence or non-occurrence of one or more future events are also disclosed as contingent liabilities unless the probability of outflow is remote.

(n) Events after the balance sheet date

Events after the balance sheet date that provide additional information about Smart Ascent Group's position at the balance sheet date or those that indicate the going concern assumption is not appropriate are adjusting events and are reflected in the Financial Information. Events after the balance sheet date that are not adjusting events are disclosed in the notes to the Financial Information when material.

5. CRITICAL JUDGEMENTS AND KEY ESTIMATES**Critical judgements in applying accounting policies**

In the process of applying the accounting policies, the directors have made the following judgements that have the most significant effect on the amounts recognised in the Financial Information (apart from those involving estimations, which are dealt with below).

Going concern basis

The Financial Information has been prepared on a going concern basis, the validity of which depends upon the financial support of the ultimate parent at a level sufficient to finance the working capital requirements of Smart Ascent Group. Details are explained in note 2 to Financial Information.

Key sources of estimation uncertainty

The key assumptions concerning the future, and other key sources of estimation uncertainty at the balance sheet date, that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year, are discussed below.

(a) *Estimation on impairment on intangible asset*

Smart Ascent Group performs annual tests of impairment on intangible asset with carrying amount of HK\$281,473,437 as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008. The recoverable amounts of cash-generating units are determined based on value-in-use calculations. These calculations require the use of estimates and assumptions made by management on the future operation of the business, pre-tax discount rates, and other assumptions underlying the value-in-use calculations. Where the actual outcome in future is different from the original estimates, such difference will impact the carrying value of the intangible asset and the impairment on intangible asset in the year in which such estimate has been changed.

(b) *Impairment loss on investments in subsidiaries*

No impairment is provided for investments in subsidiaries, which was determined according to the directors' estimation. If the financial positions of the subsidiaries are to deteriorate in the future or profitability of operations of the subsidiaries in foreseeable future is doubtful, full or partial impairment may be required and Smart Ascent's results and financial position in the future may be affected.

6. FINANCIAL RISK MANAGEMENT

Smart Ascent Group's activities expose it to a variety of financial risks: foreign currency risk, credit risk and liquidity risk. Smart Ascent Group's overall risk management programme focuses on the unpredictability of financial markets and seeks to minimise potential adverse effects on Smart Ascent Group's financial performances.

(a) **Foreign currency risk**

Smart Ascent Group has minimal exposure to foreign currency risk as most of its business transactions, assets and liabilities are principally denominated in HK\$, which is the functional currency of the principal operating entities of the Smart Ascent Group. Smart Ascent Group currently does not have a foreign currency hedging policy in respect of foreign currency transactions, assets and liabilities. Smart Ascent Group will monitor its foreign currency exposure closely and will consider hedging significant foreign currency exposure should the need arise.

(b) **Credit risk**

The carrying amount of other receivables and bank and cash balances included in the consolidated balance sheet represent Smart Ascent Group's maximum exposure to credit risk in relation to Smart Ascent Group's financial assets.

The credit risk of other receivables is further detailed in note 12 to the Financial Information.

(c) **Liquidity risk**

Smart Ascent Group's policy is to regularly monitor current and expected liquidity requirements to ensure that it maintains sufficient reserves of cash to meet its liquidity requirements in the short and longer term.

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

The maturity analysis of Smart Ascent Group's financial liabilities is as follows:

	Less than 1 year HK\$	Between 1 and 2 years HK\$	Between 2 and 5 years HK\$	Over 5 years HK\$
At 31 August 2008				
Accruals and other payables	389,987	—	—	—
Due to the immediate holding company	4,430,278	—	—	—
Due to a minority shareholder	32,403,892	—	—	—
At 31 August 2007				
Accruals and other payables	241,393	—	—	—
Due to the immediate holding company	4,010,039	—	—	—
Due to a minority shareholder	32,403,892	—	—	—
At 31 March 2008				
Accruals and other payables	560,657	—	—	—
Due to the immediate holding company	4,099,639	—	—	—
Due to a minority shareholder	32,403,892	—	—	—
At 31 March 2007				
Accruals and other payables	203,309	—	—	—
Due to the immediate holding company	3,957,641	—	—	—
Due to a minority shareholder	32,403,892	—	—	—
At 31 March 2006				
Accruals and other payables	238,127	—	—	—
Due to the immediate holding company	2,815,751	—	—	—
Due to a minority shareholder	32,403,892	—	—	—

(d) Fair values

The carrying amounts of Smart Ascent Group's financial assets and financial liabilities as reflected in the consolidated balance sheets approximate their respective fair values.

7. TURNOVER

Smart Ascent Group did not generate any turnover during the Relevant Periods.

8. INCOME TAX EXPENSE

- (a) No provision of Hong Kong Profits Tax is required since Smart Ascent Group has no assessable profits for the Relevant Periods.

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

- (b) The reconciliation between the income tax expense and the product of loss before tax multiplied by the Hong Kong Profits Tax rate is as follows:

	Year ended 31 March			For the five months ended 31 August	
	2006 HK\$	2007 HK\$	2008 HK\$	2007 HK\$	2008 HK\$
Loss before tax	(278,381)	(215,481)	(502,322)	(90,832)	(158,819)
Domestic tax rate	17.5%	17.5%	17.5%	17.5%	16.5%
Tax at the domestic tax rate	(48,717)	(37,709)	(87,906)	(15,896)	(26,205)
Tax effect of expenses that are not deductible	48,717	37,709	87,906	15,896	26,205
Income tax expense	—	—	—	—	—

- (c) No provision for deferred taxation has been made in the Financial Information as there are no temporary differences.

9. LOSS FOR THE YEAR/PERIOD

Smart Ascent Group's loss for the year/period is stated after charging the following:

	Year ended 31 March			For the five months ended 31 August	
	2006 HK\$	2007 HK\$	2008 HK\$	2007 HK\$	2008 HK\$
Auditor's remuneration	108,500	100,000	380,000	40,000	138,330
Directors' emoluments	—	—	—	—	—
Impairment loss on goodwill	20,039	—	—	—	—

10. INTANGIBLE ASSETS

Smart Ascent Group

	Goodwill HK\$	Technological know-how HK\$ Note	Total HK\$
Cost			
At 1 April 2005	—	281,473,437	281,473,437
Additions	20,039	—	20,039
At 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008	20,039	281,473,437	281,493,476
Impairment			
At 1 April 2005	—	—	—
Charge for the year	20,039	—	20,039
At 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008	20,039	—	20,039
Carrying amount			
At 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008	—	281,473,437	281,473,437

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

At 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008, the carrying amount represents the technological know-how of HK\$281,473,437 (the "Know-how") in relation to an oral insulin product (the "Product") and the exclusive right for the commercialisation of the Product owned by Smart Ascent Group. The Product was co-developed by Fosse Bio, a subsidiary acquired by Smart Ascent during the year ended 31 March 2004, and Tsinghua University, Beijing ("THU"). Fosse Bio and THU jointly applied the patent (the "Patent") in respect of the Know-how on 20 April 2001. The Patent was granted by State Intellectual Property Office of the People's Republic of China (the "PRC") and United States Patent and Trademark office of the United States of America on 4 August 2004 and 28 March 2006 respectively. The clinical trials of the Product are still in progress up to the issue date of this Financial Information. Should the approval of results of the clinical trial fail, the certificate of new medicine cannot be obtained from the State Food and Drug Administration of the PRC ("SFDA") or the launching of the Product be unsuccessful, adjustments would have to be made against the carrying amount of the Know-how.

The directors of Smart Ascent have reassessed the recoverable amount of the Know-how and considered that no impairment against its carrying amount is required as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008.

11. INVESTMENTS IN SUBSIDIARIES

Smart Ascent

	As at 31 March			As at 31 August	
	2006	2007	2008	2007	2008
	HK\$	HK\$	HK\$	HK\$	HK\$
Unlisted investments, at cost	<u>40,065,711</u>	<u>40,065,711</u>	<u>40,065,711</u>	<u>40,065,711</u>	<u>40,065,711</u>

Particulars of the subsidiaries as at 31 August 2008 are as follows:

Name	Place of incorporation and operation	Issued and paid up capital	Percentage of equity interest Direct	Principal activities
Fosse Bio (note)	Hong Kong	10,000 ordinary shares of HK\$10 each	51%	Research and development and commercialisation of oral insulin products
Welly Surplus	Hong Kong	100 ordinary shares of HK\$1 each	51%	Inactive

Note: Fosse Bio was acquired by Smart Ascent from Fordnew Industrial Limited (the "Fosse Vendor") during the year ended 31 March 2004. Pursuant to the deed of transfer (the "Deed") entered into between Smart Ascent and the Fosse Vendor, Smart Ascent acquired a 51% equity interest of Fosse Bio from the Fosse Vendor at a consideration (the "Fosse Consideration") which is payable in four installments. The first and second installments were already settled. The third installment of HK\$12,000,000 shall be paid within 14 days from the issuance of certificate of phase III clinical study of the Product issued by the SFDA. The fourth installment of HK\$19,780,000 shall be paid within 14 days from the issuance of certificate of new medicine for the Product by the SFDA. The third and fourth installments with total amount of HK\$31,780,000 are included in the amount due to a minority shareholder as at the balance sheet date and are still outstanding as at the issue date of this Financial Information. Upon Extrawell (BVI) Limited acquiring the 51% equity interest in Smart Ascent from Mr. Ong Cheng Heang and Ms. Wu Kiet Ming (the "Vendors"), the Vendors jointly and severally agreed to undertake in full the outstanding Fosse Consideration if and when the respective sum became due and payable. As a result, a corresponding amount of HK\$31,780,000 (note 12) was recorded as other receivable by Smart Ascent Group as at the balance sheet date.

12. OTHER RECEIVABLES

At 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008, included in Smart Ascent Group's other receivables is an amount of HK\$31,780,000 ("Receivable") due from Mr. Ong Cheng Heang and Ms. Wu Kiet Ming (the "Vendors"). Mr. Ong Cheng Heang is a director of Smart Ascent. Ms. Wu Kiet Ming is the daughter-in-law of a director of Smart Ascent, Mr. Ho Chin Hou. The amount represents receivable from the Vendors for the third and fourth installments of the Fosse Consideration due to undertaking by them for the acquisition of 51% equity interest in Smart Ascent by Extrawell (BVI) Limited as set out in note 11 to the Financial Information. The amount is still outstanding as at the issue date of the Financial Information. Shares representing 49% equity interest of Smart Ascent have been pledged by one of the Vendors to Extrawell (BVI) Limited for securing the settlement of the Receivable. Since the Know-how is the only major asset of Fosse Bio, which in turn is the only major investment of Smart Ascent, the value of the pledged 49% equity interest of Smart Ascent depends on the results of the clinical trials and the successful launching of the Product. As explained in note 10 to the Financial Information, should the approval of the clinical trials fail, the certificate of the Product cannot be obtained from the SFDA, or the launching of the Product be unsuccessful, adjustments would have to be made against the carrying amount of the Receivable.

Other receivables are denominated in HK\$ as at 31 March 2006, 2007 and 2008, and 31 August 2007 and 2008.

13. DUE FROM/TO THE IMMEDIATE HOLDING COMPANY/SUBSIDIARIES/A MINORITY SHAREHOLDER

The amounts due from/to the immediate holding company/subsidiaries/a minority shareholder are unsecured, interest free and have no fixed terms of repayment.

14. SHARE CAPITAL

	<u>As at 31 March</u>			<u>As at 31 August</u>	
	2006	2007	2008	2007	2008
	<i>HK\$</i>	<i>HK\$</i>	<i>HK\$</i>	<i>HK\$</i>	<i>HK\$</i>
Authorised, issued and fully paid:					
10,000 ordinary shares of					
HK\$1.00 each	<u>10,000</u>	<u>10,000</u>	<u>10,000</u>	<u>10,000</u>	<u>10,000</u>

Smart Ascent's objectives when managing capital are to safeguard Smart Ascent Group's ability to continue as a going concern, so that it can continue to provide returns for shareholders and benefits for other stakeholders, and to provide an adequate return to shareholders.

Smart Ascent Group manages the capital structure and makes adjustments to it in the light of changes in economic conditions and the risk characteristics of the underlying assets. In order to maintain or adjust the capital structure, Smart Ascent Group may adjust the amount of dividends paid to shareholders, if any, return capital to shareholders, issue new shares, or sell assets to reduce debts. No changes were made in the objectives, policies and processes during the Relevant Period.

Smart Ascent Group monitors capital using a gearing ratio, which is Smart Ascent Group's total debts (comprising amounts due to immediate parent and a minority shareholder) over its total assets. Smart Ascent Group's policy is to keep the gearing ratio at a reasonable level. Smart Ascent Group's gearing ratio was 12.6%, 13.1%, 13.1%, 13.1%, 13.3% as at 31 March 2005, 2006 and 2007 and 31 August 2007 and 2008 respectively.

15. RESERVES

(a) Smart Ascent Group

The amounts of Smart Ascent Group's reserves and the movements therein are presented in the consolidated statements of changes in equity.

APPENDIX II ACCOUNTANTS' REPORT OF SMART ASCENT GROUP

(b) **Smart Ascent**

	Retained profits <i>HK\$</i>
At 1 April 2005	39,860,280
Loss for the year	<u>(235,070)</u>
At 31 March 2006 and 1 April 2006	39,625,210
Loss for the year	<u>(179,198)</u>
At 31 March 2007 and 1 April 2007	39,446,012
Loss for the year	<u>(447,182)</u>
At 31 March 2008 and 1 April 2008	38,998,830
Loss for the period	<u>(158,819)</u>
At 31 August 2008	<u><u>38,840,011</u></u>
At 1 April 2007	39,446,012
Loss for the period	<u>(90,832)</u>
At 31 August 2007	<u><u>39,355,180</u></u>

16. NOTES TO THE CONSOLIDATED CASH FLOW STATEMENTS

Acquisition of a subsidiary

On 22 February 2006, Smart Ascent Group acquired 51% of the issued share capital of Welly Surplus for a consideration of HK\$51. Welly Surplus was inactive during the Relevant Periods.

The fair value of the identifiable assets and liabilities of Welly Surplus acquired as at its date of acquisition, which has no significant difference from its carrying amount, is as follows:

	HK\$
Net liabilities acquired:	
Bank and cash balances	706
Due from shareholders	100
Accruals and other payables	<u>(40,000)</u>
	(39,194)
Minority interests	<u>19,206</u>
Smart Ascent's share of 51% interest	(19,988)
Goodwill	<u>20,039</u>
Satisfied by:	
Due to minority shareholders	<u><u>51</u></u>
Net cash inflow arising on acquisition:	
Cash consideration paid	—
Cash and cash equivalents acquired	<u>706</u>
	<u><u>706</u></u>

The goodwill arising on the acquisition of Welly Surplus is attributable to the anticipated profitability of the distribution of Smart Ascent Group's products in the new markets and the anticipated future operating synergies from the combination.

17. COMMITMENTS

- (a) At 31 August 2008, Smart Ascent Group had a commitment to advance an interest-free loan to Fosse Vendor and/or other shareholders of Fosse Bio for expenses relating to clinical trials of the Product.
- (b) On 19 October 2006, Sea Ascent Investment Limited ("Sea Ascent"), Welly Surplus and Fosse Bio entered into a cooperation agreement (the "Cooperation Agreement") in connection with the cooperation (the "Cooperation") between Sea Ascent and Welly Surplus in respect of (i) Sea Ascent shall procure its wholly owned subsidiary, Joy Kingdom Industrial Limited ("Joy Kingdom"), to establish a wholly foreign owned enterprise in the PRC under the name of 江蘇派樂施藥業有限公司 (Jiangsu Prevalence Pharmaceutical Limited) ("Jiangsu Prevalence"); (ii) Sea Ascent shall advance a sum equivalent to RMB40 million to Joy Kingdom by way of an unsecured, non-interest bearing shareholder's loan ("Shareholder's Loan") for the payment of the registered capital of Jiangsu Prevalence and the acquisition of land and construction of a factory (the "Plant") at Pi Zhou City, Jiangsu, the PRC for the production of Smart Ascent Group's Oral Insulin Enteric-Coated Soft Capsules (the "Medicine"); and (iii) subject to Sea Ascent's performance of its obligations as aforesaid and completion of the acquisition of Joy Kingdom by Welly Surplus as mentioned below, Welly Surplus shall procure Joy Kingdom or Jiangsu Prevalence, if so agreed, to pay to Sea Ascent, during a period of six years from the date on which the Medicine is launched for sales in open market (the "Initial Operating Period"), a fee at RMB6 cents for each capsule of Medicine produced (subject to a maximum fee of RMB180 million and deduction as specified in the Cooperation Agreement). The Cooperation Agreement became effective upon the shareholders' approval in the special general meeting of the ultimate parent, Extrawell Pharmaceutical Holdings Limited, held on 3 January 2007, until the expiry of the Initial Operating Period.

On 19 October 2006, Sea Ascent and Welly Surplus also entered into a sale and purchase agreement ("SP Agreement") pursuant to which Sea Ascent agreed to sell and Welly Surplus agreed to acquire (i) the entire share capital (the "Sale Share") in Joy Kingdom and (ii) the Shareholder's Loan at considerations of RMB40 million and HK\$1 respectively (the "Consideration"). The completion of the SP Agreement was subject to, among other conditions, approval of the SP Agreement by the shareholders of the ultimate parent, Extrawell Pharmaceutical Holdings Limited, the Cooperation Agreement becoming effective and the completion of the construction of the Plant by Jiangsu Prevalence in accordance with the terms of the Cooperation Agreement. The SP Agreement was approved in the special general meeting of the ultimate parent, Extrawell Pharmaceutical Holdings Limited, held on 3 January 2007. At 31 August 2008, the SP Agreement has not yet become unconditional and the Consideration has not yet been due and paid up to the issue date of the Financial Information.

18. SUBSEQUENT EVENTS

No significant subsequent event took place subsequent to 31 August 2008.

19. SUBSEQUENT FINANCIAL STATEMENTS

No audited financial statements have been prepared by Smart Ascent or any of its subsidiaries in respect of any period subsequent to 31 August 2008.

Yours faithfully
RSM Nelson Wheeler
Certified Public Accountants
 Hong Kong

The following is the text of the report dated 21 May 2009 from 北京北醫醫療投資有限公司 (PKU Medical Investment Co.) in connection with its market report on insulin products, prepared for the purpose of incorporation in this circular. PKU Medical Investment Co. is a company established in the PRC specialised in the medical and healthcare related consultancy fields. The diabetes market report project team, which prepared this report, was led by Dr. Adam Zhao, PhD, and Dr. Jiang Long, MD, who had been the leads for several consultancy projects in the PRC, including a joint venture hospital for an Austrian Private Hospital Chain in the PRC and an investment project for Tsingdao Starwood International Heart Hospital. Please also refer to the biographies of Dr. Zhao and Dr. Jiang as set out at the end of the report.

Date: 21 May 2009

Diabetes market report

as of 28 February 2009

PKU Medical Investment Co. (PUMIC)

GLOSSARY OF TERMS AND ABBREVIATIONS

“API”	means Activate Pharmaceutical Ingredients.
“CNS”	means central nervous system.
“CE”	means Confirmatory European; an acronym for the French “Conformite Europeenne” (certifies that a product has met EU health, safety, and environmental requirements, which ensure consumer safety) for sale throughout the Europe.
“DDP4 inhibitors”	means a new class of oral hypoglycemics which block DPP-4. Their mechanism of action is thought to result from increased Incretin levels which inhibit glucagon release but more importantly increase insulin secretion and decrease gastric emptying.
“DM”	means Diabetes Mellitus.
“FDA”	means Food and Drug Administration of the USA.
“SFDA”	means the State Food and Drug Administration of China.
“Glucagon-like-peptide-1 (GLP-1)”	is derived from the transcription product of the proglucagon gene. The major source of GLP-1 in the body is the intestinal L cell that secretes GLP-1 as a gut hormone. It can 1) increase insulin secretion from the pancreas in a glucose-dependent manner; 2) decrease glucagon secretion from the pancreas; 3) increase beta cells mass and insulin gene expression; 4) inhibit acid secretion and gastric emptying in the stomach.
“GIR (Glucose Infusion Required)”	The golden standard of insulin therapeutic effect.
“Human insulin (R), NPH and Pre-combined 30R, 50R”	means various types of human insulin that exist in the market. They have different effective time, effective duration and injection frequency to meet the requirements of different diabetes patients.
“Insulin Analogues”	means an altered form of insulin, different from any occurring in nature, but still available to the human body for performing the same action as human insulin in terms of glycemic control.
“Insulin Sensitizers”	means an oral type of anti-diabetes drugs, which could stimulate the secretion of insulin in pancreas.
“IGR”	means Impaired Glucose Regulation.
“OAD”	means oral anti-diabetic drug.
“ROW”	means rest of the world.
“bn”	means billion.
“m”	means million.

INTRODUCTION

Global

With US\$24bn annual sales in 2007, treatment for diabetes generates one of the largest pharmaceutical markets, which continues to grow rapidly. It is, however, split into two large components — insulin and oral anti-diabetic drugs (OAD) — that have very different market characteristics. In addition, a new group of glucagon-like-peptide-1 (GLP-1) analogues has emerged between these groups.

The three segments of the diabetes market

	Insulin market	OAD market	GLP-1 analogues
Prescribers	Specialists	GP-driven	In between
Gross margins	Low	High	High
IP Status	No patents until analogues	Normal patents	20 years normal patents
Administration	Injections	Oral tablets	Injections
Type of the industry	Capital-intensive	Marketing-driven	Marketing-driven
Key Players	Novo Nordisk, Sanofi-Aventis, Eli Lilly	GSK, Takeda, Sanofi-Aventis	Eli Lilly, Amylin
Size in 2007	<u>US\$10.7bn</u>	<u>US\$12.7bn</u>	<u>US\$0.68bn</u>

Source: DrKW (Dresdner Kleinwort Wasserstein) Equity research

The OAD market is much like most other pharmaceutical markets. Companies develop new products based on a novel chemical entity, prove the efficacy in phase III trials and try to market the product to as wide a population as possible before patent expiry. Manufacturing tends to be simple and gross margins high. This typically leads to very rapid sales erosion after patent expiry, as is the case in most pharmaceutical industry segments.

The insulin market, by contrast, has remained essentially the same for the past 80 years. Waves of new product generation have led to evolution of the treatment into more patient-specific patterns and better injection convenience. China has developed animal insulin in 1960s but such products were replaced by human insulin in the 1970s and 1980s, and insulin analogues are currently taking over part of the market from human insulin. But the core of the treatment is still the same: patients are injected with relatively simple protein molecules that are closely related to the hormone that controls glucose levels in healthy individuals.

Despite being a biological product, insulin remained relatively cheap until the emergence of analogues. These products are modified insulin molecules. This modification can be patented. At the same time, insulin has been increasingly used in Type 2 patients as a terminal or complement treatment as well. Hence the insulin market has become rather more like the OAD market, and this transition has been the main driver of recent growth.

GLP-1 analogues products are likely to reach approximately US\$1.1bn of sales by 2010. Although their sales could fall short of the most bullish market expectations, they are likely to slow down the injectable insulin market growth, at the same time as the value increase from the switch to analogues slows down. Insulin analogues already make up almost 75% of the US insulin market value and 60% of the volume.

The market trends are summed as follows: The insulin market has experienced dramatic growth due to analogue conversion. The OAD market has faced several patent expiries. No GLP-1 analogues or inhaled insulin available.

Global diabetes market — Key forecasts

	2003 (US\$m)	2004 (US\$m)	2005 (US\$m)	2006 (US\$m)	2007 (US\$m)	2008F (US\$m)	2009F (US\$m)	2010F (US\$m)
Insulin sales	5,573	6,516	7,646	8,550	10,680	11,855	13,040	14,214
% YoY		17%	17%	12%	25%	11%	10%	9%
— Analogues	1,987	2,787	3,786	4,633	6,394	7,653	8,820	9,874
— Human insulin	3,586	3,729	3,860	3,880	3,967	4,102	4,220	4,340
— Inhaled	0	0	0	37	319	100	—	—
GLP-1 analogues	—	—	59	252	680	880	1,060	1,280
% YoY				327%	170%	29%	20%	21%
OADs	8,455	9,210	10,230	11,390	12,749	14,024	15,286	16,509
% YoY		9%	11%	11%	12%	10%	9%	8%
— Sensitizers (incl combinations)	4,182	4,781	4,994	6,263	7,369	8,259	9,253	10,188
— DPP4 inhibitors					546	1,375	2,258	3,291
Total market	14,028	15,726	17,935	20,192	24,109	26,759	29,386	32,003
% YoY		12%	14%	13%	19%	11%	10%	9%

Source: Drkw Equity Research estimates

China

China shares the same development pace with global trends in the diabetes treatment domain. According to “China Diabetes Report and Guideline (中國糖尿病防治指南) of 2006”, there are over 40m diabetes population in China for 2004, with even large IGR generates. The total market value is around USD1.1 billion for 2007, which also split into two major categories — OAD and insulin. In addition, traditional Chinese medicine plays an important role in the Chinese diabetes treatment market in terms of market occupation.

In large, the OAD takes over 50% of the total market share in terms of sales revenue, which contains around 10% Chinese traditional medicine since those drugs are all in oral type. Insulin takes almost half of the market, of which about 15% is analogues and 85% is human insulin. The GLP-1 analogues grew rapidly in recent years and there are no inhaled ones available in mainland China till now.

China diabetes market — Key forecasts

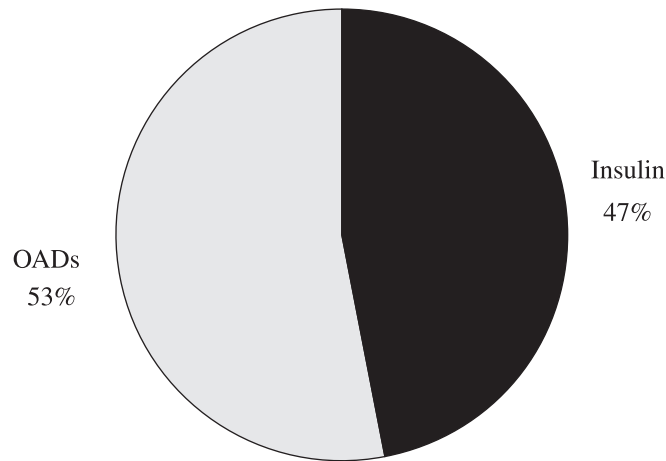
	2003 (US\$m)	2004 (US\$m)	2005 (US\$m)	2006 (US\$m)	2007 (US\$m)	2008F (US\$m)	2009F (US\$m)	2010F (US\$m)
Insulin sales	225	359	392	431	529	645	835	1,031
% YoY		60%	9%	10%	23%	22%	30%	23%
— Analogues	0	0	15	35	70	140	280	420
— Human insulin	225	359	377	396	459	505	555	611
— Inhaled	0	0	0	0	0	0	0	0
GLP-1 analogues	0	0	0	0	0	8	16	25
% YoY							100%	56%
OADs	369	410	436	499	573	661	721	818
% YoY		11%	6%	14%	15%	15%	9%	13%
— Sensitizers (incl combinations)	335	369	387	406	451	496	546	600
— DPP4 inhibitors	0	0	0	34	51	87	90	124
Total market	594	769	828	930	1,102	1,314	1,572	1,874
% YoY	N.A.	29%	8%	12%	18%	19%	20%	19%
— Traditional Chinese Medicine	34	41	49	59	71	78	85	94

Source: Credit Suisse Research, SFDA 醫藥經濟研究所

Market size and patient split forecasts

The diabetes market totaled US\$24bn in 2007 and projected to be over US\$29bn in 2009. This makes the treatment of diabetes one of the biggest pharmaceutical markets. The market is less fragmented than, eg, CNS or cardiovascular markets, and the only two segments have been insulin and OADs (oral anti-diabetic drugs) as mentioned above. Despite insulin's status as the only effective therapy for Type 1 diabetes patients and terminal treatment for Type 2 patients, insulin forms 47% of the market by value.

Global Diabetes Market — value split by treatment type 2007



Source: Market Research

What's more, the growth within the diabetes market has recently moved to insulin. The current value share of insulin is clearly higher than 47% in 2007. The insulin market has grown much faster than the OAD market. This is due to several factors:

- Patent expiries of several products (mostly OAD, eg, Glucophage, Glucotrol-XL and Glucovance) have weakened the growth of the market tremendously. In addition, the fast growing combination segment was hit in 2005 by a temporary withdrawal of Avandamet due to manufacturing problems.
- Conversion of the insulin market from human insulin to premium-priced insulin analogues increases the value of the insulin market.

The reason that why insulin analogues priced higher than human insulin is that:

- (1) Higher technology needed, so higher entry barrier for new players, less competitions.
 - (2) More patents covered, higher entry barriers and fewer players as well.
 - (3) Later developed than traditional insulin, therefore priced higher for premium profit too.
- Relatively low prices of insulin have left more room for price increases, most notably in the developing countries, like China and India.

Global diabetes market — sales forecasts by product segment

	2003 (US\$m)	2004 (US\$m)	2005 (US\$m)	2006 (US\$m)	2007 (US\$m)	2008F (US\$m)	2009F (US\$m)	2010F (US\$m)
Diabetes, total	14,028	15,726	17,935	20,192	24,109	26,759	29,386	32,003
% growth		12%	14%	13%	19%	11%	10%	9%
OAD market	8,455	9,210	10,230	11,390	12,749	14,024	15,286	16,509
% growth	—	9%	11%	11%	12%	10%	9%	8%
GLP-1 analogues	—	—	59	252	680	880	1,060	1,280
% growth				327%	170%	29%	20%	21%
Insulin market	5,573	6,516	7,646	8,550	10,680	11,855	13,040	14,214
% growth		17%	17%	12%	25%	11%	10%	9%

Source: Market Research

In addition to product mix and pricing changes, diagnosis rates are an important driver of insulin market growth. Increasing diagnosis rate in developing countries, particularly Asia, should increase the accessible Type 2 diabetes patient population dramatically. Together with the increasing use of insulin for Type 1 patients and improved survival rate the number of insulin patients in the developing world is expected to increase dramatically.

In the industrialized countries, we expect the conversion from human insulin to insulin analogues to continue to boost growth, since the insulin analogues have better patient compliance, better blood sugar controlling capability and relative higher gross margin. But the diagnosis and treatment rates in the US and Western Europe are already relatively high, close to 70%, and conversion rate of insulin to analogues has exceeded 50% of volume in the US. Also, emerging new therapies like GLP-1 analogues, as well as potential availability of two new OAD classes (DPP4 inhibitors and dual-acting sensitizers) are all negative for the insulin market growth.

We draw two main conclusions from our macro forecasts:

- In the OAD market, there is considerable room for value and volume growth, both in industrialized and in developing countries. This is driven mainly by increasing prevalence of Type 2 diabetes in industrialized countries, and by increasing diagnosis rate in developing countries.
- In the insulin market, the growth in patient numbers will continue to be rapid. However, the established manufacturers face the challenge of slowing volume and value growth in the developed countries, while growth potential in developing countries is accelerating.

China

Along with the international diabetes market booming and new products be developed domestically, the China diabetes market is also growing in full speed. OADs, which include traditional Chinese medicines, are taking over 50% of the market, while insulin and insulin analogues are catching up, since the efficiency and safety profile of human insulin is much better than the OADs.

As a developing country, China has a huge population with limited medical resources and payment capability. Also, the relative complicated injection technique prevents the population to transfer from OADs to insulin family. So the OADs market will keep growing in a steady rate along with the diagnosis rate increasing.

Global players, like Novo Nordisk and Eli Lilly, have entered China for many years, and they have helped to educate the whole market, both to the physicians and the patients, to make them better understand the meaning of sugar level controlling, pros and cons of OADs and insulin family, and how to avoid complications of diabetes. These actions not only boost their own sales number, but also helped the domestic players, like Tonghua Dong Bao (通化東寶, Shanghai-listed shares 600867.SS), to enter the huge market more rapidly.

Insulin analogues are more quick acting and stable in controlling the sugar level than insulin; also the price of insulin analogues is much higher than the gene-recombined human insulin, so the market share and total revenue of such products increase very quickly.

China has favorable medical insurance policies upon the diabetes patients. Most of the OADs and human insulin products could be reimbursement accordingly. However, some of the imported types, especially the high price formulation are not covered by the basic medical insurance system. This is a good situation to the domestic players, who always apply the low-price strategy.

Diabetes: the disease

Diabetes (or *diabetes mellitus*) is a chronic disease caused by deficiency in insulin production in the pancreas, or by failure of organs to react properly to the insulin produced. A lack of insulin results in increased concentrations of glucose in the blood, which in turn damage many of the body's organs and functions, in particular the blood vessels and nerves.

Type 1 and Type 2 diabetes

There are two principal forms of diabetes:

- **Type 1 diabetes** (previously known as insulin-dependent diabetes) in which the pancreas fails to produce insulin. Since insulin is essential for survival, this disease is often fatal. This form develops most frequently in children and adolescents, but is being increasingly diagnosed later in life as well.
- **Type 2 diabetes** (previously known as non-insulin-dependent) results from the body's inability to respond properly to the insulin produced by the pancreas. Type 2 diabetes is much more common than Type 1 diabetes, and accounts for around 90% of all diabetes cases worldwide. It occurs most frequently in adults, but is being noted increasingly in adolescents as well. The prevalence follows increasing rates of obesity and lack of exercise.

A vast majority of diabetes patients have Type 2 diabetes. However, practically all Type 1 patients are diagnosed or alternatively die at a young age due to lack of treatment. Meanwhile, within the Type 2 patient population, the diagnosis rate is much lower due to lack of diabetes-specific symptoms before the disease has progressed to an advanced stage, and not all diagnosed

Type 2 patients are treated. Both types of diabetes are complex diseases caused by a combination of environmental factors and inherited tendency. Genetic markers have been shown to increase the risk of developing Type 1 diabetes. In Type 1 diabetes the beta cells of the pancreas are destroyed, usually by an autoimmune reaction possibly triggered by an infection.

Prevalence

Data by the World Health Organization (WHO) show that approximately 246m people had diabetes globally in 2007, and that number will more than 380 million by 2025.

The overall patient statistics comes from the United Nations (UN) and WHO population and diabetes patient data projections. Interestingly, the prevalence of Type 1 diabetes is still rather low in developing countries, probably because lack of insulin leads to premature death of most patients. Truly global availability of insulin could increase the prevalence in developing countries close to the 0.5% level in industrialized countries. In the US, Western Europe and Japan, the prevalence of Type 2 diabetes in industrial countries is 5%. In the recent past, however, the most dramatic increase in the prevalence of diabetes has been in the US. Among the adult population the prevalence was 7.2% in 2007, according to Centers for Disease Control (CDC). The incidence of Type 2 diabetes has nearly doubled since 1990. The main driver of this trend is increasing obesity as a result of unhealthy diet and lack of exercise.

It is estimated that approximately 20% of the US population is obese, defined by having a body mass index (BMI) above 30, up from less than 10% in 1990. On top of that, most of the remaining population is overweight, defined by having a BMI above 25. Because about 75% of Type 2 diabetes cases are attributable to being overweight and it takes several years to develop diabetes, the full impact of increasing obesity on diabetes prevalence has not yet been felt. If the US population suddenly started becoming leaner, the diabetes prevalence would still continue to go up for several years.

China

WHO noted that much of global increase is likely to occur in developing countries (particularly China) and be due to population growth, ageing, unhealthy diets, obesity and changes in lifestyles. Also, better availability of medicines is likely to increase patient population due to better survival of Type 1 diabetes patients. According to “China Diabetes Report and Guideline (2006)”, there are over 40m diabetes population in China for the year 2004, with even large IGR generates. IGR is a very dangerous condition, because 1.5%–10% of the IGR patients will progress to diabetes in each year. The rate may increase to 13.8% if the age of the population up to 50–75. A research targets mainland China and Hong Kong indicated the IGR transfer rate of these areas ranges from 8–11% in yearly based, which is much higher than average. In 2006 the morbidity rate of diabetes and IGR in China is around 5% and 5.25%, which mean the population with insufficient sugar tolerance is over 100m.

DM Morbidity Rate in China (%)

Year	Diabetes	IGR
1980	1.00%	N.A.
1989	2.02%	2.95%
1994	2.51%	3.20%
1996	3.21%	3.81%
2006	5.00%	5.25%

Source: China Diabetes Report and Guideline

Though there are many estimations of the number of DM patients in China, most of the official estimations points to at least 5% of population as shown above. With a 1.3 billion population in China at 2006, the DM patients reach at least 60 million in China at 2006.

As for the growth of the DM population, there are even more estimations. The latest report from China Diabetes Society (www.cds.org.cn) in September 2007 indicates the growth of DM patients in China as 3,000 per day, or 1.2 million per year (www.cds.org.cn/zhinanyugongshi/HTML/20071130135807.html). However, we believe a range between 500,000 to 1,000,000 patient/year is a more reasonable number for DM patient growth in China.

A series of complications diseases of diabetes are also big problem in diabetes treatment and management. The major complications include diabetes retinopathy, kidney failure, heart disease, diabetic neuropathy, and diabetic foot disease, etc. The expense on the treatment of complications of diabetes is even bigger than the diabetes alone. The severity and progress of diabetes complications heavily depend on the sugar level which be controlled by OAD or insulin, so the basis of diabetes complications management still relies on the two category drugs that mentioned above.

DM Complication Morbidity Rate in China 2007 (%)*DM Complication Morbidity Rate in China (%)*

Type	Hypertension	Cerebral	Cardio-vascular	diabetes foot	diabetes retinopathy	kidney failure	diabetic neuropathy
DM Type 1	9.1	1.8	4	2.6	20.5	22.5	44.9
DM Type 2	37.2	11.6	17.3	5.2	35.2	34.1	66.8
Total	31.9	12.2	15.9	5	34.3	33.6	60.3

Source: China Diabetes Report and Guideline

Products and Players

Most of the other treatments try to regulate the amount of insulin released from the pancreas. Exceptions among widely used products are insulin sensitizers (glitazones) and metformin. Insulin sensitizers make the body more sensitive to insulin and metformin prevents excessive glucose

production in the liver. There are also drugs that try to prevent absorption of glucose from the intestine, but these have failed to gain significant market share. The new class of GLP-1 analogues induces glucagon-like effects when the blood sugar is too low.

Insulin

Insulin is the body's natural treatment for hyperglycemia. It is an anabolic hormone which controls take-up of glucose from the blood. Insulin remains the end-stage therapy for Type 2 diabetes and it is the only life-saving treatment for Type 1 diabetes. The insulin market was first converted from animal insulin to human insulin in the 1970s, and is currently being converted further to insulin analogues with better pharmacokinetic properties. Consequently, the insulin market is divided into two segments, human insulin and insulin analogues.

Insulin by speed/duration of action

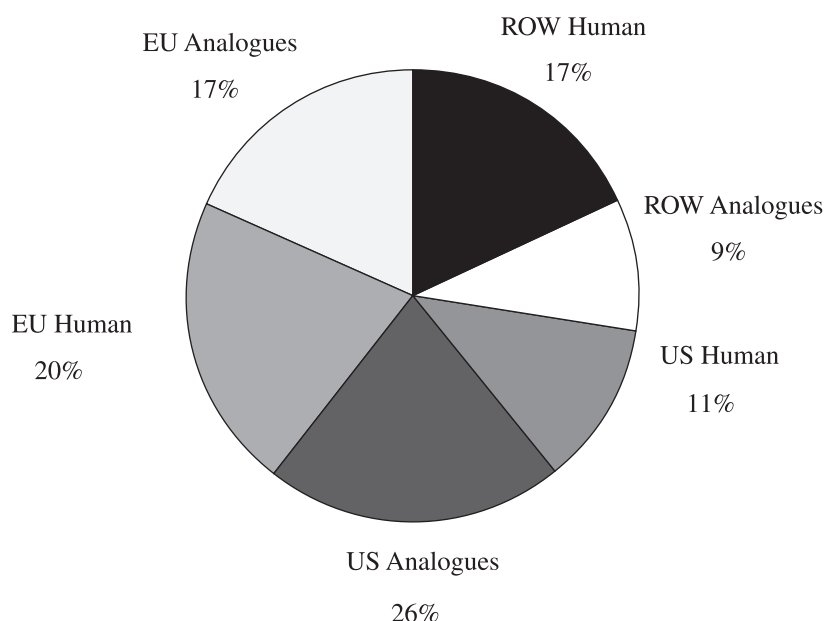
	US name	Company	Time to onset (h)	Peak (h)	Duration (h)
Short-acting insulin analogues					
	Humalog	Eli Lilly	<0.25	1	3.5–4.5
	NovoLog	Novo Nordisk	<0.25	2	3–5
	Apidra	Sanofi-Aventis			
Short-acting human insulin					
	Novolin R	Novo Nordisk	0.5	2.5–5	8
	Humulin R	Eli Lilly	0.5	2–4	6–8
	—	Sanofi-Aventis			
Intermediate acting insulins (NPH)					
	Humulin N	Eli Lilly	1–2	6–12	18–24
	Humulin L	Eli Lilly	1–3	6–12	18–24
	Novolin N	Novo Nordisk	1.5	4–12	24
	Novolin L	Novo Nordisk	2.5	7–15	22
Pre-mixed insulins					
	Humulin	Eli Lilly	0.5	2–12	24
	Novolin 70/30	Novo Nordisk	0.5	2–12	24
	Humalog Mix	Eli Lilly	<0.25	0.5–1.5	24
	Novolog Mix	Novo Nordisk	<0.25	0.5–1.5	24
Long-acting human insulin					
	Humulin U	Eli Lilly	4–6	8–20	24–48
		Novo Nordisk	4–8	16	20
Long-acting analogues					
	Lantus	Sanofi-Aventis	1	None	> 24
	Levemir	Novo Nordisk	1	None	Up to 24h

Source: Industry Data and Market Research

Both segments are further divided into different sub-segments, depending on the duration of action of the product. Current market dynamics are characterized as continuing attempts by the pharmaceutical companies to convert human insulin patients into insulin analogues. At the same time, vials are being upgraded to pens, and there is a constant battle between companies about which is the best treatment scheme for new insulin patients.

Growth in the global insulin market was 25% in 2007 to US\$10.7 billion from US\$8.5 billion the year before. In recent years, US dollar depreciation has boosted the market value when measured in dollars. Europe is now an equally large insulin market by value, partly because of the stronger euro, but also because the prices in human insulin in US\$ are lower than in Europe.

Geographical split of global US\$10.7bn insulin market 2007



Source: Market research and credit Suisse Research

The characteristics of the US and European markets are distinctively different. In the US, analogue conversion has reached much higher levels than in Europe. As the chart above shows, the US analogue market is already more than two times as big as the human insulin market (in value). Low human insulin prices in the US are a factor in this, but the volume share of the analogues is also much higher.

China

In the past 20 years, human insulin (R), human insulin NPH and pre-combined 30R and 50R have dominated the insulin market in China. Until 2005, the insulin analogues only takes 5% of the total market share, while the number in the international market is around 50–60%. There's a 5 years gap and delay in the insulin analogues development in China, but the growth rate of sales revenue will boom in the coming years due to the huge needs.

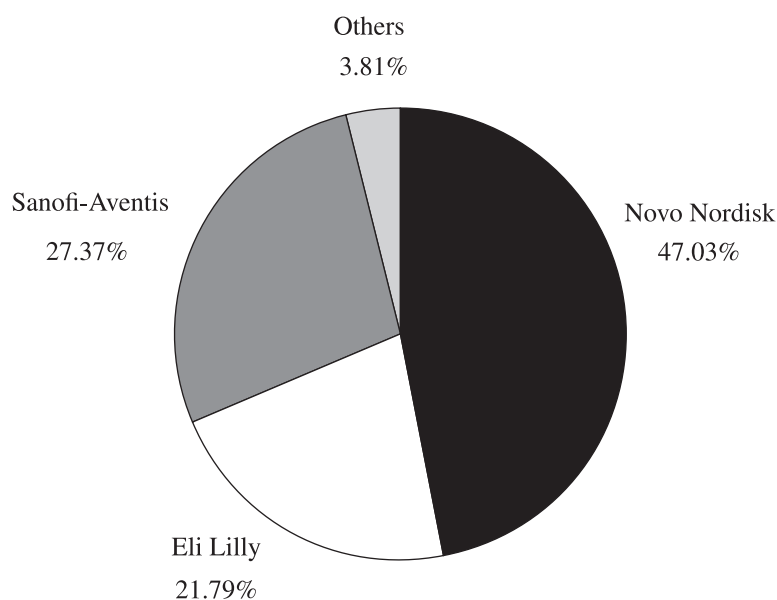
Beijing, Shanghai, Guangzhou and other developed cities contributed major sales numbers in the total market, and the numbers have been heavily influenced by “social reimbursement and insurance” system and policies. Once a product entered the system, the sales revenue would increase dramatically. By the first quarter of 2006, insulin market had been developing smoothly in the 3 major cities (Beijing, Shanghai and Guangzhou). By the second quarter of 2006, market in the above mentioned 3 large cities grew very fast, especially in Beijing. Thereafter, Shanghai and Guangzhou market entered a new steady period while fluctuation in Beijing was remarkable, climbing up dramatically in the fourth quarter of 2006. Beijing market made particularly good performance among the first class city markets. Research from Shanghai Wei Yun consulting firm showed that Insulin purchasing expense in sample hospitals in 14 cities has grown rapidly in the last 2 years. Its growth rate in 2004, 2005 and 2006 was 23%, 17% and 20% respectively. The average annual growth rate was 20.3%, which was higher than the average growth rate of total domestic anti-diabetic drugs market (13%) during the same period.

In China, the market for insulin belongs primarily to multinational corporations; say Eli Lilly and Novo Nordisk. Novo Nordisk dominates in China with approximately 62.53% of the market. Eli Lilly holds approximately 23.25% of the Chinese market. Other multinational corporation players like Sanofi-Aventis has a 7.75% market share and is aggressively seeking a more major insulin marketing position.

Novo Nordisk remains the market leader

Novo Nordisk remains the leader in the global insulin market, but Sanofi-Aventis is making strong gains in analogues with only one product, long-acting insulin analogue Lantus. Remarkably, these two companies have not previously been in meaningful head-to-head competition before this year, since Sanofi-Aventis has not launched its short-acting insulin analogue Apidra yet, and Insuman has been very small product available only in Europe.

Market share of global US\$10.7bn insulin market by company 2007



Source: Market Research and Credit Suisse Research 2008

The previous chart showing geographical split of the market also shows a meaningful opportunity in Europe of switching the patients from human insulin to insulin analogues remains. This is particularly the case for Novo Nordisk since we believe the bulk of these patients are long-acting human insulin users who Novo Nordisk has been able to retain, instead of availability of Lantus. Novo Nordisk's dominant position in short-acting analogues in Europe means that patients who wish to combine Lantus with short-acting insulin would need to combine products from two different manufacturers.

In the past several years, Sanofi-Aventis was number three behind Eli Lilly, but within insulin analogues, Sanofi-Aventis had in 2004 almost reached the analogue market leader, Eli Lilly. FY2007 figures are likely to show Sanofi-Aventis as the global market leader with the US\$3 billion revenue generated by Lantus.

Eli Lilly the main loser, but the end of decline might be in sight

Eli Lilly is consistently losing market share in every market. This has been due mainly to two reasons: (1) the roll-out of Lantus has switched many patients from long-acting human insulin into long-acting insulin analogues (a segment where Eli Lilly has no product); (2) Novo Nordisk has been very successful in the US market, after switching its focus from OADs to insulin.

Interestingly, the global diabetes model suggests that the gains of Lantus within the analogue segment have peaked. The overall US insulin analogue market continues to grow strongly, but it appears that the share of long-acting analogues as a percentage of total peaked early this year.

The market share gains of Novo Nordisk and Aventis have also been partly due to Eli Lilly's relative inactivity in the field, and the company has used this business as a cash generator. The recent change in share of long-acting analogues could provide a first hint of a change in favor of Eli Lilly; particularly should the human insulin market have entered a new period of accelerating growth in 2005. Reactivation of Eli Lilly is a logical step after launching Byetta in 2005 and ahead of expiry of the Takeda/Actos deal in 2011.

China

Tonghua Dong Bao (通化東寶) Pharmaceutical Co Ltd is penetrating the local market and kept gaining market share from the duopoly in China

Tonghua Dong Bao (通化東寶) is the leading domestic insulin and insulin analogues products maker in China. The company has developed the human insulin in 1998 and insulin analogues in 2001, of which can compete with Eli Lilly and Novo Nordisk in terms of the quality and stability. Though the sales price of Tonghua Dong Bao's products is only 60–70% compared with the duopoly, the sales revenue has increased dramatically to RMB90 million in 2006. The 2007 market share of 甘舒霖 (Human insulin formulation) is around 2.8% of the total insulin market in China.

Tonghua Dong Bao has developed the most popular long-acting insulin analogues, named 長秀霖, recently. Though the current market share for such products is still low, but the organic growth rate is around 40%, both in the international market and the domestic market.

The company is also an insulin API producer, who exports insulin quick freeze powder to US and Europe. With the expanding phase II manufacture facility, the production capacity will increase to 3000kg/per year, which is 500% to the current number. The company has received certificates from the FDA and CE marks by European Countries on the API and countries of south Asia and Russia on the formulations.

Tonghua Dong Bao holds several key intellectual properties, like gene-recombination patents chain and PEG decoration technology; therefore the company can well protect its leading position in the domestic market.

Other domestic players

Shenzhen Kexing (深圳科興) has developed the human insulin in 2002, named 蘇泌林. Xuzhou Wanbang Pharma (徐州萬邦) has developed the human insulin in 2003, named 萬邦林. However, the market shares for those companies are too small and have little influence to the entire market structure.

Conclusion: Competition likely to increase globally

Until now, the insulin market has never really seen any form of competition other than a mini-monopoly or a duopoly in western markets. There has been some movement of patients between segments, but within each segment, competition has been limited.

Globally speaking,

- Short-acting analogue markets and pre-mixed insulin markets have been a duopoly between Novo Nordisk and Eli Lilly
- Human insulin market has also been near-duopoly, with Aventis as a third (minor) player in Europe
- Long-acting analogue markets have been a monopoly of Sanofi Aventis until 2005

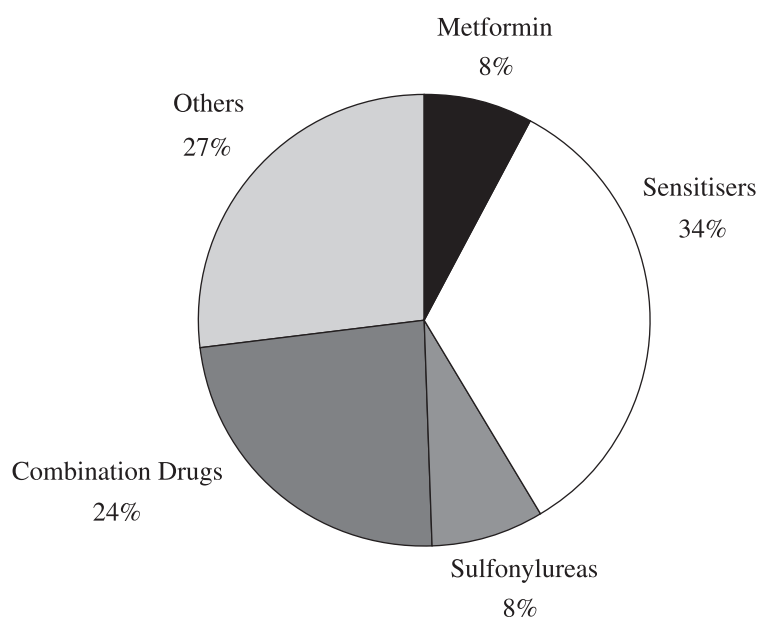
For China,

- Domestic players are gaining the market share from international players
- Insulin analogues will be most likely to copy the sales of the international market as it will gradually replace similar market share of traditional insulin market.

OADs (Oral antidiabetic drugs) at a glance

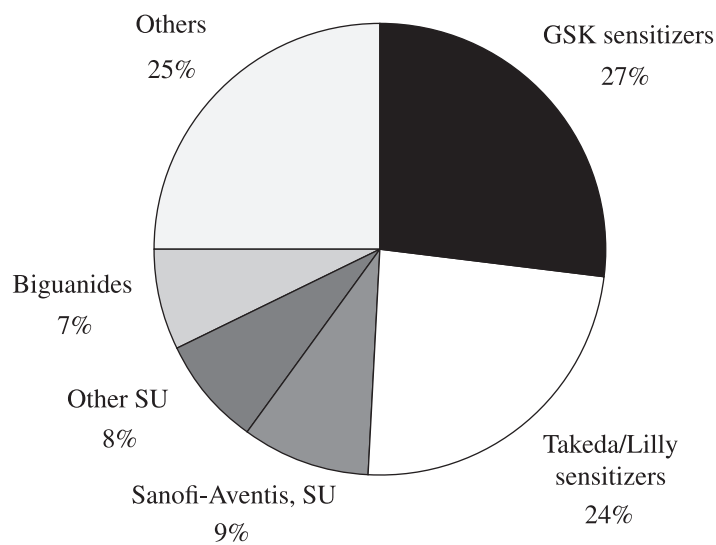
While the insulin market has been an oligopoly split between Novo Nordisk, Eli Lilly and Sanofi-Aventis, the OAD market has been much more fragmented. It also has much more in common with the big traditional pharmaceutical markets like blood pressure, CNS and ulcer. The products are oral and prescribed by general practitioners (GPs). The main drug classes in the OAD market are sulfonylureas, biguanides (in practice only one drug, metformin), and insulin sensitizers.

Global US\$12.7bn OAD market by product class in 2007



Source: Market Research

Totaled US\$12.7bn in 2007, the OAD market remains attractive for new drugs. Due to the growing number of Type 2 diabetes patients in developed countries, the market has been an optimal target for the traditional blockbuster business model. In value terms, the fastest growth has recently been reported in the insulin sensitizer segment, which also received some positive news this year. New data showed these drugs generated cardiovascular benefits in long-term use. Meanwhile, metformin and sulfonylureas (SUs) have suffered from patent expiries. Companies that are active in the market include GSK, Takeda/Eli Lilly, Sanofi-Aventis, Pfizer, Novo Nordisk and Novartis, among others. Due to success of sensitizers, GSK and Takeda/Eli Lilly are clear market leaders globally.

OAD market — Key players

Source: Market Research

New ones expected to enter are Novartis, Roche, AstraZeneca and Merck. These companies, however, rely on new product classes. The key late-stage development projects in OAD largely fall into two new drug classes: DPP4 inhibitors (Novartis, Merck, Roche, GSK) and dual-acting inhibitors (AstraZeneca, BMS, GSK).

Recent news on either of these classes is not good: After promising phase II data, Novartis published weaker-than-expected phase III results of LAF-237, the leading DPP4 inhibitor. It is also becoming increasingly likely that the dual-acting sensitizer class is very risky although several compounds remain in development after a couple of high-profile dropouts. Dual-acting indicates the drug is targeting both too high blood sugar levels and often too high lipid levels for type 2 diabetes patients. The Food & Drug Administration (FDA) required more safety data on this type of oral drugs before approving.

In China, most of the domestic OAD drugs are generic ones. Some of traditional Chinese medicine, like the well known 消渴丸, have great sales records before, but are losing their market share along with the recognition and concept updating of the formal diabetes treatment way in the Chinese population.

MAIN BRANDS IN INSULIN

Human insulin

Genetically produced human insulin was launched in the early 1980s and it replaced animal insulin almost completely in the early 1990s. Prior to this, purified bovine or porcine insulin had been used, but there were problems with immunogenicity in the animal-derived insulin products. Animal insulin has refused to completely die out; it continues to be used in the developing world and for those patients who have problems in using human insulin.

There are different subtypes of human insulin with different pharmacokinetic profiles. The differences between the human insulin variants are smaller and predictability weaker than in the case of analogues, but the split between short-acting and long-acting insulin has always been an elemental part of the insulin market. The long-acting formulations have typically been made by forming suspension of human insulin with zinc or protamine.

Humulin (優泌林) (Eli Lilly)

Humulin is the short-acting human insulin product by Eli Lilly. There are several versions of Humulin. Humulin R is regular human insulin, identical to natural human insulin, while Humulin N (NPH human insulin) is a crystalline suspension of human insulin with protamine and zinc, providing longer activity profile. Humulin L (Lente) and Humulin U (Ultralente) are formulations that have an even longer activity profile than Humulin N. Humulin is available globally, although the bulk of sales are generated in Eli Lilly's home market, say US. Humulin is also available in premixed versions. However, in October 2005, Lilly disclosed plans to discontinue Humulin U Ultralente and Humulin L Lente from the market. This is because most of Lilly's sales in the long-acting segment have long been in Humulin N, and because Lantus has taken market share in the most long-acting product segment. This will probably lead to a one-off jump in analogue conversion rates as these patients are partially switched to Lantus.

Actrapid/Novolin (諾和靈) (Novo Nordisk)

Actrapid (Europe)/Novolin (US) are Novo Nordisk's brand names for its human insulin products among several other European brand names. In the US, product names have a nearly identical logic to those of Eli Lilly. Novolin R is regular insulin while Novolin N stands for NPH insulin. Novo Nordisk, however, has not had products comparable with Humulin U in the US market. In the ex-US markets, Actrapid corresponds to Novolin R, Insulatard is the brand name for Novolin N and Monotard and Ultratard are longer-acting versions.

Insuman (Sanofi-Aventis)

Insuman was relaunched by Aventis in 1999. The product is not available in the US, but it was launched in Japan in 2001. There are long-acting, short-acting and mixed formulations of the product.

甘舒霖 (Tonghua Dong Bao 通化東寶)

Tonghua Dong Bao estimates that the insulin market in developing countries will reach US\$1bn this year. Recombinant human insulin product 甘舒霖 was launched in China in 1998 and the company is eventually planning expansion into US and Europe. 甘舒霖 is a recombinant human insulin, with the special characteristic of being expressed in E.Coli, as opposed to yeast that are used by the largest manufacturers, like Novo Nordisk. Even if the product eventually could enter the Western world, 甘舒霖 will initially focus in China and other third-world countries, where the regulatory requirements are lowest, there is most need for low-cost insulin and more than half of the market (in volume) is still estimated to be bovine or porcine-derived insulin. Eventually, we believe that entry to Western markets is likely, but Tonghua Dong Bao obviously needs a marketing partner.

Short-acting insulin analogues

Short-acting insulin analogues are molecules that are chemically almost identical to insulin. However, they are slightly modified to change their pharmacokinetic profiles. These changes have typically no effect on the efficacy of the molecule, or on the binding of insulin analogues to the insulin receptors.

Humalog (優泌樂) (Eli Lilly)

Humalog (insulin lispro) was the first short-acting insulin analogue to be launched in the US after approval in 1996. The product was introduced to European markets the same year and in Japan 2001. Humalog is a modified human insulin molecule in which two amino acids at positions 28 and 29 (lysine and proline) are reversed. Humalog was shown to have identical potency with human insulin on a molar basis, ie, one unit of Humalog has the same glucose-lowering effect as one unit of human insulin, but the effect is more rapid and of shorter duration. As the first insulin analogue to be launched, Humalog had to fight an uphill battle in gaining market share. The main benefits stressed were faster action, ie, there is no need to take insulin before a meal, but insulin analogues can be taken in connection with meals. When taken in connection with meals, Humalog results in lower postprandial glucose than Humulin R, Eli Lilly's short-acting human insulin.

NovoRapid/NovoLog (門冬胰島素) (Novo Nordisk)

NovoRapid (insulin aspart, called NovoLog in the US) is a short-acting insulin analogue that has a structure almost identical to human insulin. However, an amino acid (proline) is replaced with another (aspartic acid) in the insulin molecule. This change reduces the tendency of insulin molecules to form dimers and hexamers. The single isomer has a faster absorption profile, but the receptor properties of the insulin molecule remain unchanged. As a result, the product has an almost immediate effect and can be taken just before a meal. NovoRapid was launched in Europe in 2000 and the next year in the US. US sales really took off only in early 2003, after Novo Nordisk switched marketing focus from OADs to insulin and introduced NovoLog Mix 70/30 premixed insulin and launched the disposable administration devices FlexPen and InnoLet. The launch in Japan occurred in 2001. There have been few attempts to differentiate the short-acting analogues on the basis of product profiles because the companies have been focusing on converting the human insulin users to analogues. However, Novo Nordisk has benefited from the perceived superiority of Novo's injection devices.

Apidra (Sanofi-Aventis)

Apidra (insulin glulisine) will be the third in the market of short-acting analogues. Like other short-acting analogues, the insulin molecule of the short-acting analogue Apidra has been slightly modified (two amino acids in the case of Apidra) to reach faster onset of action and shorter half-life, relative to human insulin. Sanofi-Aventis has also demonstrated lower glucose levels and higher insulin levels than Humalog. Apidra was approved in 2004 and has been launched first in European markets this year.

The US launch will follow shortly, but the Japanese market is expected to require more clinical studies. Key problem in the launch has been several problems with the injection device.

速效霖 (Tonghua Dong Bao 通化東寶)

Tonghua Dong Bao introduced the 速效霖, a kind of Recombinant Human Insulin Lispro Injection formulation, to the China market in 2001. The product competes with the Humalog (Eli Lilly) directly with much lower price. Eli Lilly has raised a series of lawsuits upon the intellectual properties of Tonghua Dong Bao in year 2005, but the final results favored Tonghua Dong Bao and made their production and sales of 速效霖 legally in China. Tonghua Dong Bao also needs to improve their delivery system to better penetrate the domestic market.

Premixed insulin analogues

Premixed insulin analogues are combinations of short-acting insulin analogues and longer-acting insulin. Only Eli Lilly and Novo Nordisk have premixed insulin in the market. The premixed analogues have two phases of absorption. The early phase represents the rapid onset of short-acting insulin analogue. The late phase represents the prolonged action of insulin suspension.

Premixed insulin is used almost exclusively for Type 2 diabetes patients. These patients often start their insulin treatment with premixed insulin formulations to make the treatment schedule easier, eg, the patients need to carry only one product with them, and they need to use only one type of administration and injecting devices.

Humalog Mix (Eli Lilly)

Humalog Mix is a mixture of insulin lispro solution and insulin lispro protamine suspension. The protamine suspension is a suspension of crystals produced from combining insulin lispro and protamine sulphate under appropriate conditions so that slow-dissolving crystals are formed. Humalog Mix was originally launched as Humalog Mix 70/30 formulation, but in 2001 Eli Lilly started selling Humalog Mix 75/25 that has a faster onset of action. Currently most sales are Humalog Mix 75/25.

NovoMix/Novolog Mix (Novo Nordisk)

NovoMix is biphasic insulin aspart, comprising soluble insulin aspart and protamine crystallised insulin aspart. The first available formulation was NovoMix 30, which has 30% soluble insulin and 70% crystallised form. Novo Nordisk has also recently got approval for NovoMix 50 and 70. These products will be linked to the introduction of a new three times daily concept of diabetes treatment.

Long-acting insulin analogues**Lantus (來得時) (Sanofi-Aventis)**

Lantus is the first long-acting insulin analogue to reach the market. It was launched in Germany in 2001 and in the US and the UK later in the same year. The product has been rolled out globally, after Aventis solved the initial problems of manufacturing capacity by expanding a manufacturing plant in Germany. Currently Lantus is the leading insulin brand in the world. As is the case with short-acting analogues, the amino acid sequence has been altered, this time to prolong the half-life. This creates more predictable basal insulin that can be complemented by injections of short-acting insulin or taking OADs in connection with meals.

Lantus has a 24-hour peak-less profile and once-daily administration. The patients need to take Lantus at the same time every day, but the time can be any time during the day. Like Apidra, Lantus led to a patent dispute with Novo Nordisk, which was resolved by Aventis paying Novo Nordisk several payments during 2003–04.

Levemir (Novo Nordisk)

Levemir is Novo Nordisk's response to the challenge of Lantus, and we argue one of the most interesting innovations in insulin therapy recently. The product is human insulin with an added fatty acid. This increases binding to albumin, and consequently makes the half-life longer. In other words, the product is already evenly distributed in the blood, but is activated slowly and predictably. Clinical use is probably dominated by once-daily administration because the efficacy does not disappear suddenly at 20-hour intervals. Also, there are several advantages that Novo Nordisk can use. These include more predictable effect and weight loss associated with Levemir. Levemir was approved and launched in Europe in 2004 and the US in 2006.

長秀霖 (Tonghua Dong Bao 通化東寶)

Tonghua Dong Bao introduced the 長秀霖, a kind of Insulin Glargine Injection formulation, to the China market in 2006. The product is very similar to the Lantus and Levemir. Tonghua Dong Bao holds a unique patent in manufacturing the product, which will not infringe the rights of Novo Nordisk and Sanofi-Aventis. Also, the 長秀霖 is covered by basic medical insurance system in some of the provinces in China.

Insulin complement

SYMLIN injection was manufactured by Amylin in US, and was approved by the U.S. Food and Drug Administration on 16 March 2005. It is a synthetic analog of human amylin, a naturally occurring hormone that is made in the beta cells of the pancreas. It is approved to use toward patients with type 1 and 2 diabetes patients toward glucose control after meals. Clinical studies demonstrate that SYMLIN helps patients achieve lower blood glucose after meals, leading to less fluctuation during the day, and better long-term glucose control (A1C) compared to patients taking insulin alone. On average, patients in these studies used less mealtime insulin and also had a reduction in body weight compared to patients taking insulin alone.

Appendix:

Global diabetes market forecast by product class

	2003 US\$m	2004 US\$m	2005 US\$m	2006 US\$m	2007 US\$m	2008E US\$m	2009E US\$m	2010E US\$m
Diabetes, total	14,028	15,726	17,935	20,192	24,109	26,759	29,386	32,003
% growth		12%	14%	13%	19%	11%	10%	9%
— US	7,694	8,157	8,840	10,349	12,204	13,748	15,505	17,464
— China	594	769	828	930	1,102	1,314	1,572	1,874
— ROW	6,334	7,569	9,095	9,843	11,905	13,011	13,881	14,539
OAD market	8,455	9,210	10,230	11,390	12,749	14,024	15,286	16,509
% growth		9%	11%	11%	12%	10%	9%	8%
— US	5,657	5,767	5,847	6,604	7,751	8,611	9,629	10,664
— China	369	410	436	499	573	661	721	818
— ROW	2,798	3,443	4,383	4,786	4,998	5,413	5,657	5,845
— Biguanides	1,061	622	545	487	428	367	352	338
% growth		-41%	-12%	-11%	-12%	-14%	-4%	-4%
— US	628	210	153	114	73	29	30	31
— ROW	433	412	392	373	355	338	322	307
— Sulphonylureas	1,523	1,499	1,451	1,132	989	880	790	708
% growth		-2%	-3%	-22%	-13%	-11%	-10%	-10%
— US	638	587	516	350	297	261	229	193
— ROW	885	912	935	782	692	619	561	515
— Sensitisers (excl combinations)	3,500	4,001	4,716	4,542	4,316	4,495	4,670	4,833
% growth		14%	18%	-4%	-5%	4%	4%	3%
— US	3,015	3,391	4,053	3,768	3,437	3,497	3,537	3,543
— ROW	485	610	663	774	879	998	1,133	1,290
— DPP4 inhibitors					546	1,375	2,258	3,291
% growth						152%	64%	46%
— US					546	916	1,506	2,194
— ROW						459	752	1,097
— Combination products	682	780	278	1,721	3,053	3,764	4,583	5,355
% growth		14%	-64%	519%	77%	23%	22%	17%
— US	676	721	150	1,471	2,504	3,007	3,522	4,122
— ROW	6	59	128	250	549	757	1,061	1,233
— Other OAD, generics	1,689	2,308	3,240	3,508	3,417	3,143	2,633	1,984
% growth		37%	40%	8%	-3%	-8%	-16%	-25%
— US	700	859	975	902	893	901	807	781
— ROW	989	1,449	2,265	2,606	2,524	2,242	1,826	1,203
GLP-1 analogues	—	—	59	252	680	880	1,060	1,280
% growth				327%	170%	29%	20%	21%
— US				252	591	732	878	1,022
— China	0	0	0	0	0	8	16	25
— ROW				—	89	148	182	258
Insulin market	5,573	6,516	7,646	8,550	10,680	11,855	13,040	14,214
% growth		17%	17%	12%	25%	11%	10%	9%
— US	2,036	2,390	2,994	3,493	3,962	4,561	4,997	5,578
— China	225	359	392	431	529	645	835	1,031
— ROW	3,537	4,126	4,652	5,057	6,718	7,294	8,043	8,636
— Insulin analogues	1,987	2,787	3,786	4,633	6,394	7,653	8,820	9,874
% growth		40%	36%	22%	38%	20%	15%	12%
— US	1,221	1,635	2,162	2,675	2,993	3,338	3,772	4,213
— ROW	766	1,152	1,624	1,958	3,401	4,315	5,048	5,661
— Human insulin	3,586	3,729	3,860	3,880	3,967	4,102	4,220	4,340
% growth		4%	4%	1%	2%	3%	3%	3%
— US	815	755	831	795	763	763	763	763
— ROW	2,771	2,974	3,029	3,085	3,204	3,339	3,457	3,577
— Inhaled insulin				37	319	100	—	—
% growth					762%	-69%	NA	NA
— US				24	206	50	0	0
— ROW				13	113	50	—	—

Source: DrKW Equity research

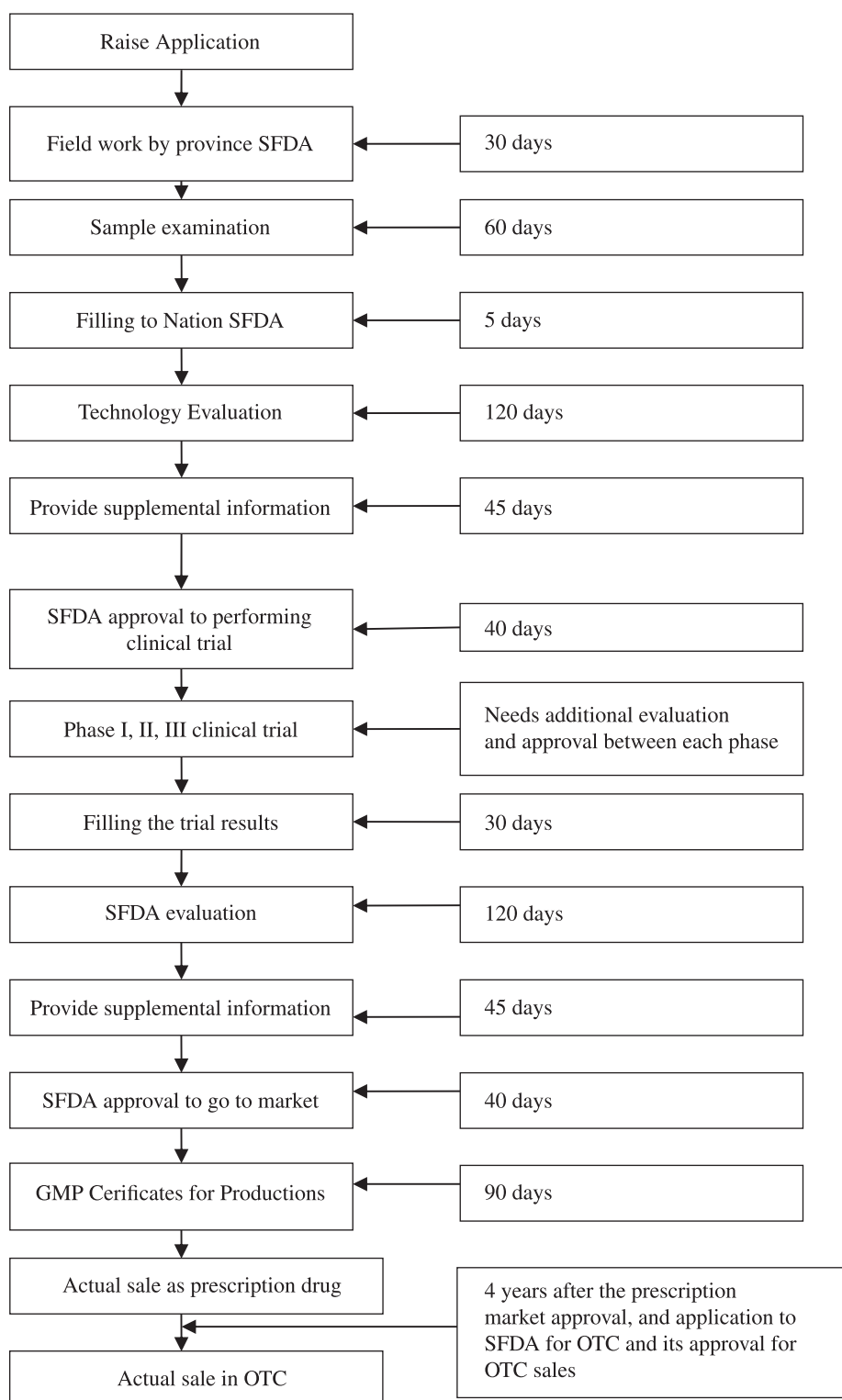
Company forecasts (in local currency)

Forecasts in local currency

	2003	2004	2005	2006	2007	2008F	2009F	2010F
Novo Nordisk								
<i>DKrm</i>								
— Human insulin	14,492	14,383	15,004	13,452	12,572	13,594	12,948	12,219
— Insulin Analogue	2,579	4,507	7,070	9,946	14,008	15,766	18,928	22,334
— OADs	1,440	1,643	1,664	1,703	1,812	1,781	1,309	1,279
Total	18,511	20,533	23,738	25,101	28,392	31,141	33,185	35,832
	5%	11%	16%	6%	13%	10%	7%	8%
Sanofi-Aventis								
<i>€m</i>								
Lantus	487	836	1,198	1,781	2,031	2,210	2,587	2,901
Apidra	0	0	0	102	257	319	395	479
Amaryl	596	684	675	457	392	288	204	166
Insuman	176	168	164	164	161	156	150	143
Total	1,259	1,688	2,037	2,504	2,841	2,973	3,336	3,689
	20%	34%	21%	23%	13%	5%	12%	11%
GSK								
<i>£m</i>								
Avandamet	92	267	94	204	292	438	657	854
Avandaryl	0	0	0	41	50	60	72	86
Avandia	839	847	1,281	1,399	877	1,087	1,127	1,173
Total	931	1,114	1,375	1,644	1,219	1,585	1,856	2,114
	2%	20%	23%	20%	-26%	30%	17%	14%
Eli Lilly								
<i>US\$m</i>								
Humulin	1,060	998	945	925	985	1,105	1,123	1,140
Humalog	1,021	1,102	1,189	1,299	1,474	1,590	1,477	1,559
Byetta	0	0	123	219	330	472	878	1,022
Total	2,081	2,100	2,257	2,443	2,789	3,167	3,478	3,721
	13%	1%	7%	8%	14%	14%	10%	7%
Pfizer								
<i>US\$m</i>								
Glucotrol XL	347	83	34	20	20	21	22	23
Exubera	0	0	0	0	0	0	0	0
Total	347	83	34	20	20	21	22	23
	2%	-76%	-59%	-41%	0%	5%	5%	5%
TongHua Dongbao								
(通化東寶)								
<i>RMB(m)</i>								
甘舒霖	0	230	277	293	323	390	520	899
長秀霖	0	0	0	0	0	25	55	89
Total	0	230	277	293	323	415	575	988
	N.A.	N.A.	20%	6%	10%	28%	39%	72%

Source: DrKW Equity research and corporate annual reports

SFDA approval process of new drugs in China



TRENDS IN INSULIN DELIVERY SYSTEM INTRODUCTION

In today's era, insulin delivery by alternative route is an area of current interest in the design of drug delivery system. A lot of biotechnology and pharmaceutical companies are showing encouraging progress in their attempts to develop alternative insulin delivery technologies.

For most patients with diabetes, the tedious part of the treatment is to tolerate needle after needle, both for glucose measurement and to deliver insulin. The introduction of insulin therapy years ago has saved the lives of millions of patients with diabetes, while the developments of technologies in the last decade have brought to limelight in turning non-injectable insulin delivery from theory to reality.

Rigorous research efforts have been undertaken worldwide to replace the authentic subcutaneous route by a more accurate and non-invasive route. Considerable progress has been made to achieve new milestones for effective treatment of diabetes. Per oral, buccal, nasal, and pulmonary administration has demonstrated good potential for treatment of diabetes. In addition, transmucosal, buccal, ocular, rectal, and vaginal routes of insulin have also shown to decrease serum glucose concentrations.

Needle Free Technology

The demand for novel drug delivery technologies is ever increasing. These drug delivery technologies can be broadly classified into four principal routes like oral, transdermal, inhalation, and parenteral. The main goal for the delivery of any drug therapy is oral administration with once or twice daily dosing since it is the most popular way of drug intake, hence most easily accepted by patients. However, there is large number of therapies, particularly protein-based, gene-based; vaccine-based that cannot be delivered by this route for example insulin, growth hormones and other similar biologics. Pulmonary delivery is another non-invasive alternative method that is suitable for small molecules and proteins. However, for drugs with very large molecular weights, such as monoclonal antibodies, penetration through the lung for systemic delivery may require some type of transport enhancement mechanism, of which there are several still at the primordial research stage. Therefore, most protein-based drugs are still being developed as injectables for initial market launch.

The diabetes market, and particularly insulin development is a hotbed for new ideas in drug delivery. It is difficult to think of any other therapeutic area, let alone another single disease, where so many factors align to drive the development of novel delivery systems. For some, especially those suffering from chronic diseases requiring injectable products two or three times a day, this process is an ongoing reality of daily life for example diabetics-accepted, but always with the hope that something new will replace the ritual of needle insertion.

To overcome the problems related to needle based injections, there is one technology that has received considerable attention during the past few years and that seems to offer all of the sought after benefits is — **Needle Free Injection Technology (NFIT)**. In general, needle-free injection technology works by forcing liquid medication at high speed through a tiny orifice that is held against the skin. This creates an ultra-fine stream of high-pressure fluid that penetrates the skin without the use of a needle. High-pressure delivery could potentially damage fragile molecules, such as monoclonal antibodies. Successful delivery of such molecules, therefore, requires a device with carefully controlled power nuances. Several companies are involved in development of this technology, which includes, Antares Pharma Inc, Aradigm Corporation, Bioject Medical Technologies Inc and Biovalve

Technologies Inc. This technology achieved the FDA approval in 1996 for the subcutaneous delivery of insulin and is CE marked. This system has been used to give thousands of successful injections without the use of a needle.

Micro-needle

Advances in the processing of materials on a micro-scale have led to the development and introduction of devices that employ very small needles — micro-needles — that have significant potential in devices for diagnostics, healthcare monitoring and drug delivery by mechanically perforating the outer skin layer and allowing for transdermal drug absorption or fluid sampling.

These processing techniques incorporate one or more technologies that enable the precise machining, extrusion, casting, and/or forming of from one to an array or grid of micro-needles. Several factors — include an aging patient population, biological drug therapies for chronic conditions, and an emphasis on patient self-monitoring and self-care — are driving an evolution in the way that healthcare is delivered. Evolving micro-needle systems will be well-positioned to address a significant segment of the large molecule biological drugs expected to emerge from the convergence of automated discovery and genome mapping. Before micro-needles find widespread use, researchers must perfect the techniques for optimally inserting them into the skin, and complete the integration of micro-needles into a full diagnostic, monitoring or drug delivery system.

This is another hot-spot in the insulin delivery research field, but few of the products have been introduced to the market with good safety and efficiency profile, due to the large molecular weight of insulin.

Insulin inhalers

Inhaled insulin appears to be a non-invasive, well-tolerated and liked modality of treatment with potential for both Type 1 and Type 2 diabetes. Results of short-term studies indicate that glycemic control achieved with an inhaled insulin regimen is comparable with a subcutaneous insulin regimen in patients with Type 1 and Type 2 diabetes patients. It has been determined in patients with Type 1 and Type 2 diabetes that improvement in overall patient satisfaction with inhaled insulin is rapid and sustainable compared with conventional subcutaneous insulin, and the reduced treatment burden has a positive impact on psychological well-being. Inhaled insulin greatly enhances patient satisfaction, quality of life and acceptance of intensive insulin therapy in a diabetic patient.

German researchers first introduced the idea of inhalable insulin in 1924. Years of failure followed until scientists realized they might be able to use new technologies to turn insulin into a concentrated powder with particles sized for inhalation. Nektar Therapeutics of San Carlos, California developed this technology that paved the way for pharmaceutical companies to begin testing and formulating inhalable insulin. Once concrete methods were developed, human tests began in the late 1990s. In January 2006, the FDA approved the use of Exubera which is a form of inhalable insulin developed by Pfizer.

Exubera

Exubera is the brand name of first formulation of inhalable insulin to receive the FDA approval. It is manufactured by Pfizer in collaboration with Nektar Therapeutics and is licensed for use by both Type 1 and Type 2 diabetics. However in the UK its use is under the National Health Service “*should*

not be recommended because it could not be proven to be more clinically or cost effective than existing treatments”, except under special circumstances. In April 2006, the UK’s National Institute for Health and Clinical Excellence (NICE) issued a preliminary statement advising against the use of inhalable insulin on the grounds that the benefits of avoiding injections did not justify the higher cost of the new product. At that time, NICE recommended use of the new drug only in clinical trials.

Concerns have been expressed by the Institute for Safe Medication Practices (A nonprofit organization educating the healthcare community and consumers about safe medication practices) about a serious risk of dosing errors when prescribing Exubera. Insulin is traditionally prescribed in international units, but Exubera is prescribed in milligrams. 1 mg of Exubera is equivalent to 3 units of insulin; however, the increment is not linear: 3 mg of Exubera is equivalent to 8 units of insulin and not 9 units as might be expected, and the prescriber is strongly advised to refer to the manufacturer’s conversion table before prescribing. Furthermore, because of retention of blister contents, three consecutive doses of 1 mg blisters of Exubera results in a higher dose of insulin than a single 3 mg blister of Exubera, further complicating prescribing calculations.

Exubera is considered short or rapid acting insulin. In clinical studies, Exubera reached peak concentration levels faster than some insulin administered by injection. Thus, this form of insulin would begin working within the body faster than insulin that is injected. Type 1 and Type 2 diabetics will still need an injection of longer acting insulin to maintain a basal level for a 24 hour period.

As of 18 October 2007, Pfizer has announced that it will no longer manufacture or market Exubera. According to Chairman and CEO Jeffrey Kindler this is because Exubera “failed to gain acceptance among patients and physicians.”

Lung cancer concerns

On 9 April 2008, Pfizer announced in its “Dear Dr.” letter that Exubera may have been associated with lung cancer: of the 4,740 patients who used Exubera in clinical trials, six have developed lung cancer as of April 2008, compared to only one of the 4,292 patients in the placebo group. The association was not statistically significant, and Pfizer maintained in its letter that “Exubera remains a safe and effective medication.”

In a letter 18 June 2008, Pfizer informed UK doctors of the above mentioned six cases, noting that they all had a prior history of cigarette smoking and that they were planning to investigate further the “observed imbalance in diagnosed lung cases” with an international observational trial. Pfizer’s letter also stated that Nektar had stopped searching for a new marketing partner and therefore Pfizer would withdraw its marketing authorization around September 2008.

In general, withdraw of Exubera by Pfizer is a big blow to the market of inhaled insulin, but not necessarily a complete negative factor for insulin market with alternative delivery route, especially potential oral insulin market. Most of the issues for Exubera are lung related, including the awkward inhaled device, additional costs for the monitor of lung function, and the concerns for lung cancer, makes it a hard product for the market to accept. Oral delivery of insulin circumstances these concerns and has the potential to solve these issues if the clinical results look promising. With the withdraw of Exubera by Pfizer, it eliminates a major competitor and might clear up the way for the future development of oral insulin.

Other Inhaled Insulin that under developing and their fate

More recently, the worldwide insulin market leaders, Novo Nordisk and Eli Lilly have tried to temper expectations for their own inhaled insulin product, which the companies anticipated bringing to market by 2009 or 2010. In January 2008 and March 2008, Novo and Eli Lilly announced to discontinue development of AERx and AIR Insulin respectively. It's starting to look like this idea was one of the biggest traps in drug marketing history.

AERx (Novo Nordisk): In 14 January 2008, Novo Nordisk announced that based on a detailed analysis of the future prospects for inhaled insulin and a review of the medical and commercial potential of the AERx[®] iDMS inhaled insulin system (AERx[®]), Novo Nordisk has decided to refocus its inhaled insulin activities and discontinue all further development of AERx[®]. To note, the decision to discontinue the development of AERx[®] is not due to safety concerns.

Lars Rebien Sørensen, president & CEO of Novo Nordisk said: "The AERx[®] system has been developed for delivering fast-acting insulin in connection with meals, and we have concluded that fast-acting inhaled insulin in the form it is known today is unlikely to offer significant clinical or convenience benefits over injections of modern insulin with pen devices such as Novo Nordisk's FlexPen[®]. In general, people with Type 2 diabetes start insulin therapy with long-acting or premixed insulin, and experience shows that they want very simple, very convenient devices for administering their insulin. This requires a completely new approach to inhalation of insulin."

Though they claim that Novo Nordisk will increase research and development activities targeted at inhalation systems for long-acting formulations of insulin and GLP-1, but people know that the trend in inhaled insulin has been blocked.

AIR Insulin (Eli Lilly): 7 March 2008, Eli Lilly announced the termination of development of its AIR(R) Insulin program, which was being conducted in partnership with Alkermes, Inc. The program has been in phase III clinical development as a potential treatment for Type 1 and Type 2 diabetes. The company noted that this decision is not a result of any observations during AIR Insulin trials relating to the safety of the product, but rather was a result of increasing uncertainties in the regulatory environment, and a thorough evaluation of the evolving commercial and clinical potential of the product compared to existing medical therapies.

Lilly's decision represents the third inhaled insulin program to be terminated by a large pharmaceutical company since October 2007 (Pfizer pulled Exubera in October 2007 and Novo Nordisk discontinued development of AERx in January 2008).

The withdrawing of big pharmaceutical companies from this market will definitely influence the whole market and some ramifications of this development will be influenced also.

AIR Insulin (Alkermes): The Company is the co-developer of Eli Lilly in AIR insulin. The event removes one of Alkermes' latest stage opportunities, though it is not one of the material drivers of valuation for Alkermes.

Technosphere® Insulin System (MannKind), currently in late stage clinical trials around the world, represents a novel drug delivery system that facilitates the rapid delivery of active ingredients to the bloodstream via the pulmonary route. The repercussions of Lilly's decision may be most negative for MannKind, a pure play inhaled Insulin Company.

For now, Technosphere® is the only inhaled insulin that is under developing.

NGI (Nektar): While Nektar already paid the price for Exubera's commercial failure; Lilly's news could damage its efforts to re-partner the much maligned product and/or NGI (next generation Exubera).

In Sum

Inhaled insulin is simply a new delivery technology for an old drug, insulin. Yet as the market failure has demonstrated, managed-care payers are no longer dazzled by new technology of itself. New technology matters only when it produces breakthroughs in treatment outcomes, hence raising the standard of care, and comes at an overall cost that's competitive with other alternatives.

Oral Insulin

The formidable task of administering insulin orally has been pursued over the last several decades with a view to helping ease the pain and stress caused during delivery of insulin injections to the millions of diabetic patients worldwide. An over-ambitious desire to deliver insulin orally has prompted many scientists to explore the various possibilities of improving the availability of insulin inside body through oral intake (namely, oral bioavailability of insulin), with in vitro and in vivo studies in animal models. Insulin is a peptide drug, hence is still a challenging and uncompromised drug molecule that cannot currently be given in oral dosage form. The barriers that may have a detrimental impact on oral absorption of insulin include poor permeability across the intestinal walls and the presence of proteolytic enzymes in intestinal flora, which is instrumental in degrading protein including the insulin molecule. In the last several decades, various strategies have been employed to overcome the formidable barriers of oral bioavailability of insulin and poor absorption.

During recent years, many other hormonal drugs such as vasopressin, which are available in an intranasal spray, success with oral insulin delivery becomes a little more encouraging. However, significant progress has been reported for delivering insulin using buccal and just recently through oral routes as well.

Approaches taken for oral insulin

Most of the studies conducted have focused mainly on enhancing the stability of insulin molecules using chemical and/or natural penetration enhancers or absorption promoters such as bile salts, surfactant and chelating agents to enhance the permeability of the intestinal mucosa and protect insulin against intestinal enzymes. In one such approach, insulin is entrapped in liposomal preparation with a view to improving oral absorption. Various carrier systems such as nano-spheres and micro-spheres were also used in conjunction with insulin to improve oral bioavailability. Some studies were focused on coating the insulin preparation with enteric polymeric materials.

It is evident from these studies that the inclusion of enhancers/promoters and/or enzyme inhibitors does expedite the diffusion of insulin molecule across the epithelial membrane in some level. Regrettably, in most of the approaches described here, still, only a small amount of insulin is absorbed in oral administration. This option represents long-term possibilities for insulin delivery, but difficulties in securing adequate blood insulin concentrations are yet to be overcome.

Oral Insulin Players Overview

The following companies are market leaders in the field of oral (both buccal and oral) insulin:

Generex Biotechnology (buccal)

Generex is a Canadian company who engaged in the research, development, and commercialization of drug delivery systems and technologies. Generex has developed a proprietary platform technology for the delivery of drugs into the human body through the oral cavity (with no deposit in the lungs). The company's liquid formulations allow drugs typically administered by injection to be absorbed into the body by the lining of the inner mouth using the proprietary RapidMist™ device.

The Company's flagship product, oral insulin (Generex Oral-lyn™), which is available for sale in Ecuador for the treatment of patients with Type-1 and Type-2 diabetes and which was approved for sale in India in October 2007, is in various stages of clinical development around the world. The Company announced that the global Phase III clinical trial of Generex Oral-lyn™ has commenced in the USA, Canada, Russia, The Ukraine, Romania, Bulgaria and Poland.

Generex's Oral-Lyn is a liquid formulation of human insulin that is sprayed into the mouth using its proprietary RapidMist device. In mouth the insulin is absorbed via the buccal mucosa, an area with a rich vasculature. Generex believes that Oral-Lyn will provide an effective alternative to insulin injections and improve patient compliance with insulin therapy.

Approval of Oral-Lyn by the Ecuadorian Ministry of Public Health was based on data from clinical trials conducted in Ecuador which involved more than 250 patients with Type 2 diabetes. These showed that Oral-Lyn had comparable efficacy to insulin injections in this patient population.

The company is also hoping to extend use of Oral-Lyn in Ecuador to Type 1 diabetic patients and has already initiated a six-month study of its safety and efficacy in adolescent and young adult patients with Type 1 diabetes. An earlier short-term study, in which Oral-Lyn was compared with short-acting subcutaneously injected pre-prandial insulin (Humulin), was considered successful. In this study Oral-Lyn was taken both before and after each meal. The real test of the product's viability, however, will come from large-scale trials involving several thousand patients that is required by regulatory authorities in North America and Europe, and currently is underway.

Generex has an agreement with insulin giant Eli Lilly for future co-marketing. Earlier September 2008, biotechnology company Shreya Lifesciences had entered into an agreement with the Generex Biotechnology Corp to market Oral-lyn, the first needle-free insulin for Indian.

However, buccal intake insulin is very different from oral insulin, in pharmacodynamic/ pharmacokinetic processes, including absorption route and effective sites. Insulin taken via buccal is absorbed through the capillary blood system inside the mouth, and will first go through blood system before it is used by the body. The buccal intake is very similar to blood injection in this aspect, which has the benefit of easy absorption into the blood system. However, insulin taken via oral will be absorbed through portal vein, where it will stop first inside liver before it is released into blood system. Though the oral insulin might have poor absorption than buccal insulin into the blood system, some researchers argue that oral insulin will take its hypoglycemic action in the liver before it is released into the blood system, which will be discussed further in the following section.

Nobex Corporation (Oral)

Nobex Corporation has centered its focus on modification of native insulin molecules to deliver a bioactive conjugate form of insulin to achieve success in reducing blood glucose levels in laboratory animal species and Type 1 diabetic patients. This work concentrates mainly on developing a conjugate insulin form hexyl insulin mono-conjugate to improve the oral bioavailability of insulin in the Type 1 diabetic population. Nobex had a strategic alliance with the India insulin giant Biocon for oral insulin co-development in 2004. However, after the failing of one of its critical relationship with GSK, the company went bankrupt and some assets including its technology with oral insulin were auctioned and subsequently acquired by Biocon around the beginning of 2007.

Biocon (Oral)

Established in 1978, Biocon Limited is one of India's premier biotechnology companies and a fully integrated biotechnology enterprise, specializing in biopharmaceuticals, custom research, clinical research and enzymes. Biocon is the first company to have commercialized the large-scale manufacture of human insulin in India, and currently one of the biggest biotech firms there. Initially, Biocon had a strategic alliance with Nobex Corporation in 2004. When the assets of Nobex were auctioned in 2007, Oral insulin is one of the intellectual property (IP) assets of Nobex acquired by Biocon. Biocon's oral insulin candidate has polymers added at specific locations in the B chain of the insulin to prevent insulin from getting destroyed in the stomach.

Biocon's leading oral insulin candidate IN-105 is a new molecule that was developed by Biocon at its facilities in Bangalore. The molecule is stable at room temperature, according to the company, making it easy to store. Besides being needle-free insulin, this method of delivery allows IN-105 to be delivered into the body in a physiological manner that mimics the way that the pancreas release insulin into the circulation (i.e. into the portal vein), similar to the oral insulin developed by Fosse Bio which will be described below. This contrasts with all the other known methods of delivery, including inhaled insulin, which brings in insulin from the periphery into the circulation.

With its approval from the Swedish medical authorities to carry out early stage human studies for this molecule in Sweden, it has entered the clinical trial of European market. On 8 September 2008, Biocon announced the results of an ascending dose study with IN-105 at the European Association for the Study of Diabetes (EASD) meeting in Rome. The study involved dosing Type 2 diabetes subjects with single doses of 0 mg (placebo), 10 mg, 15 mg, 20 mg and 30 mg tablets

of IN-105 in 5 separate periods before a mixed 600 kcal breakfast. The outcome measurements were the safety and tolerability of IN-105, as well as the pharmacokinetics and pharmacodynamics of IN-105. The results showed that IN-105 was safe and well tolerated by patients.

“The data presented here show that insulin can be reliably delivered in individuals with type 2 diabetes via the oral route. Further the administered insulin improved control post meal plasma glucose without causing symptomatic hypoglycemia. Such data support the feasibility of oral insulin delivery as a therapeutic option” said Prof Alan D. Cherrington, Ph.D. Professor of Molecular Physiology & Biophysics, Professor of Medicine, Vanderbilt University.

However, what will really determine its clinical efficacy is the next study that will have HbA1c (a measure of blood sugar control over three months) as the end point, says Harish Iyer, head (research and development) at Biocon. With the encouraging results from IN-105, Biocon is planning to launch its oral insulin drug in India by 2010.

BioSante Pharmaceuticals (Oral) and other related firms

In a development around April 2003, BioSante Pharmaceuticals presented positive results from its calcium phosphate (CAPOral) delivery system for the development of an oral insulin formulation. The results suggested that the oral insulin formulation CAPIC™, when tested in diabetic mice and normal rats, could reduce blood glucose levels. However, the project was basically terminated by the firm after the withdrawal of Exubera from the market. Similar situation happened to other firms which used to develop oral insulin, such as Coremed, Emisphere Technologies, and iMEDD. They have either terminated their projects with oral insulin development or exited the market altogether.

There are several other India biotechnology firms who claim to develop oral insulin project beside Biocon. One of them is **Transgene Biotek Ltd.** who recently announced that it has acquired a US patent for a nano-particulate carrier delivery technology for the development of oral insulin. However, there is little information about its technology and clinical development.

Other Insulin Delivery System and Methods:

Implantable insulin pumps:

An **insulin pump** is a medical device used for the administration of insulin in the treatment of diabetes, also known as continuous subcutaneous insulin infusion therapy. The device includes:

- the pump itself (including controls, processing module, and batteries)
- a disposable reservoir for insulin (inside the pump)
- a disposable infusion set, including a cannula for subcutaneous insertion (under the skin) and a tubing system to interface the insulin reservoir to the cannula.



An implantable insulin pump works the same way as an external insulin pump with two major differences:

1. It is implanted just under the skin (usually in the abdominal area) and insulin is delivered into the peritoneal cavity not into the subcutaneous tissue.
2. Using special, highly concentrated insulin, implantable insulin pumps have to be refilled every 2 to 3 months depending on the insulin requirements of the patient. Currently, implantable insulin pumps are used in selected centers in some countries in Europe by specialist doctors.

Transdermal patch:

The Altea Therapeutics PassPort™ System was the first product in development shown in FDA phase I clinical trials to provide a non-invasive, controllable and efficient way to deliver insulin via a patch on the skin. The PassPort™ System enables fast, controlled drug delivery without the pain of an injection or the possible complications associated with inhaled medications. It also avoids the first-pass gastro-intestinal and liver metabolism that occurs often after oral administration.



The PassPort™ System is comprised of an applicator (on the left) and a reservoir patch; the latter is placed on the skin and provides for painless delivery of insulin

The PassPort™ System is comprised of an applicator and a reservoir patch; the latter is placed on the skin and provides for painless delivery of insulin. The insulin transdermal patch maintains constant basal levels while avoiding skin depots of insulin common with subcutaneous injections. As a safety feature, if a patient begins to experience the hypoglycemia associated with an inadvertent overdose of insulin, they may simply remove the insulin transdermal patch, thus immediately ending the influx of insulin.

Another Israel company, named ViaDerm, has also developed similar technology, and the system is under phase II clinical trial.

Islet cell transplant:

In contrast to conventional insulin treatment, islet transplantation is far superior for achieving a constant normal glycemic state and avoiding hypoglycemic episodes. Insulin-producing beta cells are taken from a donor's pancreas and transferred into a person with diabetes. Once transplanted, the donor islets begin to make and release insulin, actively regulating the level of glucose in the blood. However, it is a surgery currently only applicable to Type 1 diabetes patients who can't be managed with insulin therapy.

FOSSE BIO-ENGINEERING DEVELOPMENT LTD (福仕生物工程有限公司) (FOSSE BIO)

The company:

Fosse Bio is a leading oral insulin formulation developer in China, who owns the oil-based self-emulsifying technology that can deliver the insulin in a safety oral route. The company has a strategic relationship with the Department of Biological Sciences and Biotechnology, Tsinghua University in developing the novel insulin delivery system. After many years of experiments, the researchers in Department of Biological Sciences and Biotechnology, Tsinghua University (Tsinghua) have discovered a novel process (mostly through different lipid component and mixing process) of delivering protein into human blood stream through digestive system, a technology with a huge potential in protein drug delivery.

The technology:

The major issue for protein drug through oral delivery is the protection of the protein during it was delivered through digestive track, whose function is to digest protein before it is absorbed into blood stream. Researchers in Tsinghua have discovered a process of forming a fine micro-emulsion particle by combining protein with lipids, which can protect protein inside from digestion while help it absorbed into the blood stream through digestive track. In the *in vitro* experiments, the Fosse Bio's insulin formulation can form fine micro-emulsion with a droplet size of about 260 nm when introduced into water under mild agitation. The result was published in an article on *China Pharm. J.* 2007, Vol 42, No. 17 pp1320 and several other journals.

Various tests have been launched to evaluate the performance of stability, absorption, transportation capabilities, and bioavailability in vitro and vivo. In the conclusion, researchers from State Key Laboratory of Bio-membrane and Membrane Biotechnology, Department of Biological Sciences and Biotechnology, Tsinghua University indicated that "A novel formulation with the capacity of encapsulating insulin was prepared. The high efficacy of blood glucose control of this formulation

was attributed to such possible positive factors as degradation resistance, permeation increase and so on. Stability, efficacy and safety of the preparation make it a promising oral formulation to achieve optimistic bioavailability.”

For example, below is the stability result of the capsule produced by Fosse Bio.

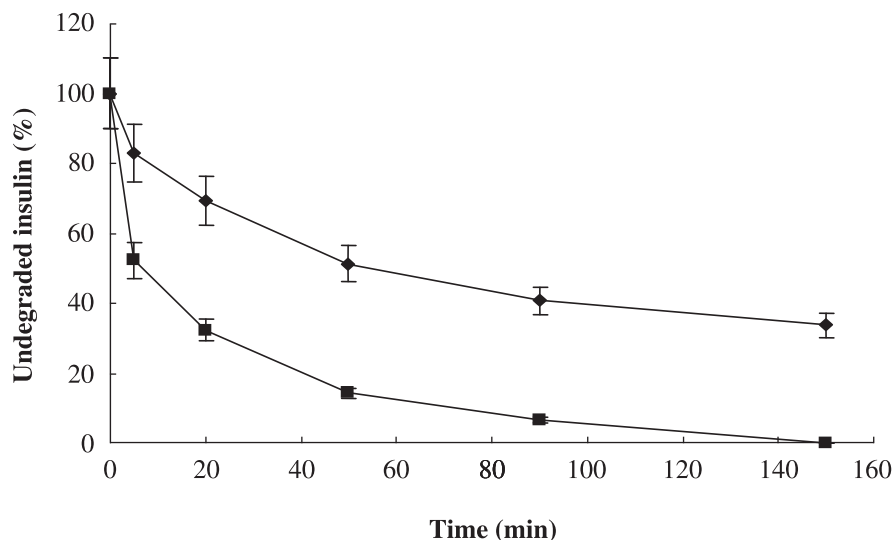


Figure 1. Degradation profiles of native insulin (■), solubilized insulin (◆) incubated with trypsin.

The degradation profiles of native insulin and encapsulated insulin in the formulations are shown in Figure 1. More than 80% native insulin was rapidly degraded within 1 hour. In contrast, the encapsulated insulin displayed a significantly higher resistance to proteolysis, which is the major agent for protein degradation.

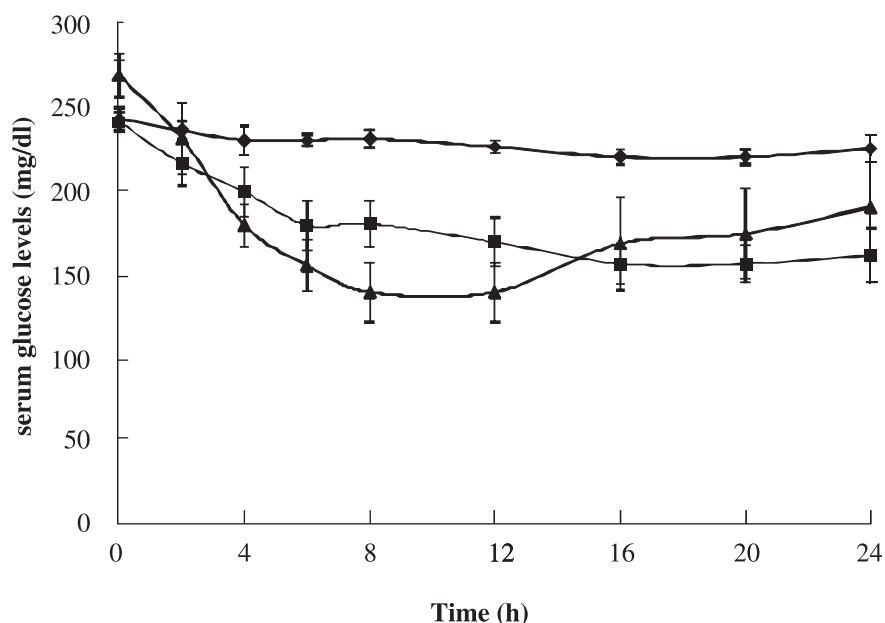


Figure 2. Reduction in serum glucose levels in the diabetic Beagle dogs. ◆, blank; ■, oral insulin 2.5 unit/kg; ▲, injectable insulin 0.5 unit/kg.

From animal research, it is found low glucose levels were maintained throughout 24 hour period. Compared with the hypoglycemic percent of native insulin administered subcutaneously, along with the unit/kg used (2.5 unit/kg for an 80% effect vs. 0.5 unit/kg for an 100% effect), the bioavailability of the oral insulin reached 15% of injectable insulin. In addition, a sustainable release was found in the diabetic dogs, when administrated with oral insulin formulation. The results from the animal research suggested that oral insulin might act with an effect as long-acting insulin, to increase the basal level of insulin, such as Lantus which is the current leading insulin analogue from Sanofi-Aventis for long-acting effect which we have described before.

Based on the above experiments, Fosse Bio and Tsinghua University jointly applied for the patent in respect of the technologies in 2001. The patent was granted by State Intellectual Property Office of the PRC and United States Patent and Trademark Office of the United States on 4 August 2004 and 28 March 2006 respectively, both having a term of 20 years from date of the application of the patent.

The clinical trials:

With the research results from Tsinghua University, this formulation was approved by the China State Food and Drug Administration (SFDA) to enter clinical trials in 2003. Fosse Bio has finished phase II multi-center clinical trial in mainland China in 2006. According to the official phase II clinical report, the insulin droplets could be released into the intestine of human beings from the capsule successfully. From the experiment, though little insulin gets into the blood stream, about 7% of injectable insulin, but they are about 25% relative bio-efficacy (based on reduction in blood sugar level) as injectable insulin, which is quite effective for oral insulin. Beside the effect on blood sugar level, the insulin capsule can also decrease the level of HbA1c by 0.98% (a measure of blood sugar control over three months), which is a significant improvement compared with other anti-diabetes drugs. However, there are some different explanations between the SFDA inspectors and clinical researchers toward one of the major findings from the clinical trials below:

Since the clinical trial used injectable insulin as comparison, the following two figures show the comparisons of blood insulin levels and effect of the drug after administration between injectable insulin and oral insulin from Fosse Bio.

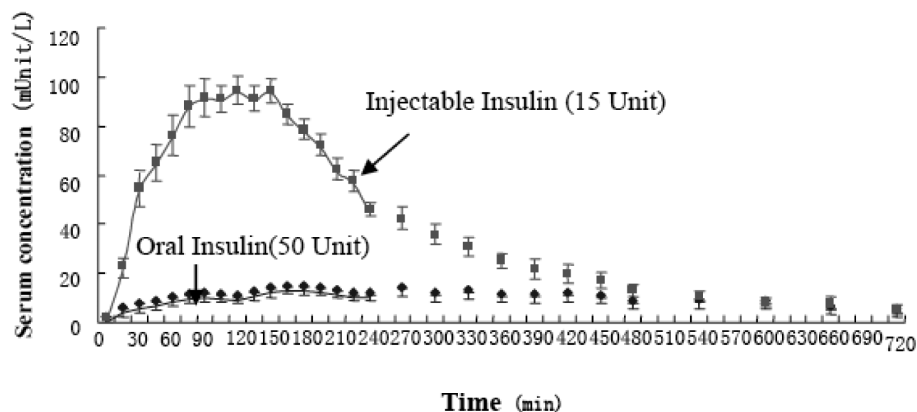


Figure 3. The average blood drug level from 20 testees with oral and injectable insulin

Figure 3 compares blood insulin level between injectable insulin and oral insulin from Fosse Bio. It shows that blood insulin level is significantly lower for oral insulin than injectable insulin.

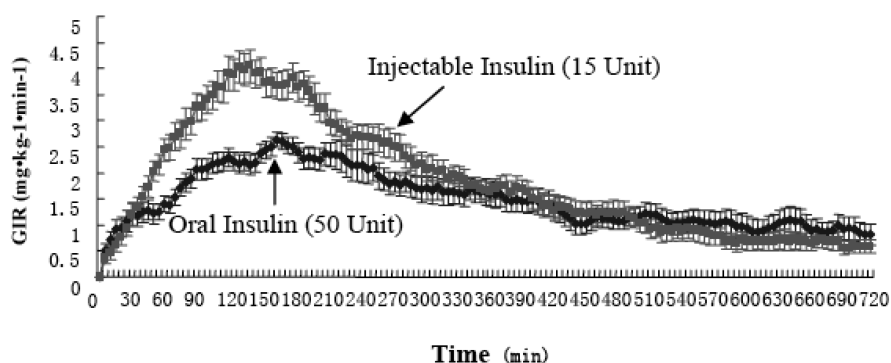


Figure 4. The average GIR-time curve for 20 testees with oral and injectable insulin

Figure 4 compares the drug effect (in term of GIR, Glucose Infusion Required, which is the golden standard of insulin therapeutic effect) of injectable insulin and oral insulin from Fosse Bio. It shows that the oral insulin has a comparable though lower, but long-lasting effect than injectable insulin.

Initially, oral insulin was expected to be regarded as degree 4 in drug development, when only the change in delivery method of drug intake was considered. It was classified as degree 2 drug and based on the requirements, Fosse Bio and Tsinghua were granted the approval from SFDA to undertake the phases I & II clinical trials. However, when the clinical results were presented to SFDA, there were different opinions from SFDA in explanation of the results. Some inspectors from SFDA queried that only small amount of insulin got into the blood stream through oral delivery, which is shown from the Figure 3, and the result from the Figure 4 only shows the psychological effect of the experiment toward diabetes patients. However, other researchers including those from Fosse Bio presented a different explanation toward these experimental results: oral insulin delivers the drug insulin into the portal vein blood stream toward the liver first, which is the major location of its therapeutic effect and also the major organ catabolizing it, before it was mostly digested (about 40% to 60% of the insulin should have been degraded in the liver) and released into the peripheral blood stream, where it is detected from the experiment. They believe the low blood insulin level of figure 3 and high therapeutic effect of figure 4 clearly support their theory.

One of the major reasons for this discrepancy between the researchers from Fosse Bio and SFDA arises from the original clinical trials required by SFDA, which are lack of double-blind experiments. It was not necessary from the original requirements from SFDA, but seems crucial for the approval of this drug with current policy from SFDA. Per the latest discussion with SFDA, the oral insulin from Fosse Bio was categorized into degree 2 new drug development which is regarded as more novel way of drug development, hence has a much higher standard of approval process.

The drug degree system from the SFDA for registration requirements was categorized as the following:

Degree 1 as new chemical entity never marketed in any country around the world.

Degree 2 as drug with changed administration route, and not marketed in any country around the world.

Degree 3 as drug marketed outside of China.

Degree 4 as drug with changed acid or alkaline radical modifications (or metallic elements), but not pharmacodynamic changes.

Degree 5 as drug with changed dose form, but no change on administration route, and the original preparation already approved in China.

Degree 6 as active pharmaceutical ingredient for drug approved by China.

Basically, the lower degree a drug belongs to, the more strict requirements will be given from the SFDA for its clinical approval.

Current situations and Future requirements:

It is noted that oral insulin was originally expected to be regarded as degree 4 in drug development whereas only the delivery method was changed for drug intake. When it was categorized as a degree 2 drug, Fosse Bio & Tsinghua worked for almost another two years to complete all the researches needed by degree 2 drug application so as to apply for the clinical trial license. In 2003, Fosse Bio & Tsinghua successfully got the phases I & II clinical trials license from SFDA and carried out the designed requirements of the phases I & II clinical trials accordingly and that double-blind test was not a requirement throughout these clinical trials. However, when the clinical results were presented to SFDA, due to the withdrawal of Exubera from the market and other internal reasons within SFDA, SFDA is very cautious in approving the non-injection type insulin formulations. From the previous clinical experiments, SFDA concluded the results inconclusive. SFDA has already required Fosse Bio to take further phase of clinical trial to compare this oral insulin with the injectable insulin and a double-blind test to further get the full picture of its safety and efficiency profile. Though this phase is not defined as II or III by SFDA, they have promised that this will be the last trial required before this drug gets to the market or not.

On 5 August 2008, we had a meeting with the SFDA officials including one of the major inspectors for endocrine or metabolic disease related drug approval where diabetes drug belongs, to discuss the approval of this drug. He admitted the lack of knowledge from SFDA about the clinical requirements of this drug when it initially sought an approval, and consequently the design of the clinical trials. However, he pointed out the value of the previous two clinical trials, including identifying the true value of this oral insulin as enhancement of basal insulin level instead of replacement of injectable regular insulin. Mainly because of the results and knowledge learned from these two clinical trials, SFDA was able to approve the following clinical trial. With the current strict standard from SFDA, this is already a big achievement. This further trial cannot be simply categorized into phase II or phase III since it comprises some additional preclinical data, and further dosing requirements which are

normally required in phase II and phase III in addition to other experiments. With a convincing result from this further clinical trial, this oral insulin drug can be an enormous achievement for Chinese pharmaceutical industry.

Currently, Fosse Bio is preparing the additional clinical data which will help to outline the scope of this additional clinical trial, which will definitely include a double-blind trial and some preclinical experiments as well. Under the current regulation process, the estimated time in total to complete the further trial and get the approval from SFDA will be 18 to 24 month, and the estimated consumption to support the further trial will be around RMB10–12 million. It is our strong recommendation that Fosse Bio to retain a third party CRO (Clinical Research Organization, which is outsourcing firms performing clinical trials for their clients) to perform the majority part of this clinical trials. This will not only ensure the correct design of the trial, but also the virtuous results from the trial, which will be critically important for the acceptance of diabetes market in the future.

In addition to the additional cost and time required for this further clinical trial, the clinical indication of the oral insulin from Fosse Bio will be amended as well. The initial indication of the oral insulin is for the replacement of the injectable regular insulin. However, the clinical results failed to show that the oral insulin is equivalent or better than the injectable regular insulin in connection with meals (short-acting insulin), which is hardly achievable, but is required for the approval of any replacement drug. With the addition of lipid formulation, the effect of the oral insulin from Fosse Bio is more like long-acting insulin analogue such as Lantus, the insulin analogue manufactured by Sanofi-Aventis. With the approval from SFDA on its clinical results of the further clinical trial, it can be marketed like Lantus, and acts as a long-acting insulin product, in the future. The new indication that the oral insulin will be pursuing is to enhance basal insulin level, as the long-acting insulin analogue such as Lantus that can be complemented by injections of short-acting insulin or taking OADs in connection with meals. This adjustment of indication, if approved, will make this oral insulin a more auxiliary role instead of replacement of injectable insulin. It will be available to both Type 1 and Type 2 diabetes patients; hence a much bigger market, but more like a supplementary drug toward a fundamental treatment as it enhances the basal insulin level for the patients. However, the potential customers will need to be educated with the positive concept and benefits of enhancing basal insulin level to protect their pancreatic islets with the input of more marketing effort. Therefore, the significance of this new adjustment toward the valuation of the oral insulin from Fosse Bio needs to be observed depending on the success of the new clinical trials, and a wider education toward diabetes patients.

With the latest incidence of dairy products tainted with melamine in China, SFDA has tighter the regulations of food inspection processes. There are some concerns that this tightened regulation might potentially delay the approval process of oral insulin from Fosse Bio. We don't believe there will be much effect because of the following reasons. Drug regulation and food inspection are completely different processes though they are under the same roof of SFDA. Traditionally, drug regulation has much tighter restriction than food regulation in SFDA, as it is the same situation around the world. With any incidences of food contamination including the recent ones, SFDA might take some measures from drug regulations to use them toward food inspections, but it should have no material effect for drug approval process. Therefore, it is our professional opinion that our estimation of approval process for oral insulin from Fosse Bio will continue to be the same. We have also obtained the confirmation from the SFDA official about this as well. In addition, the main component, insulin, for the oral insulin from

Fosse Bio is manufactured by Jiangsu Wanbang Pharmaceutical firm in China, which is the biggest insulin manufacture site in China, and one of the most trusted name in insulin production, with insulin products used widely in China and abroad.

When the oral insulin product from Fosse Bio is ready to launch in 2010, with the approval from SFDA and positive results from the latest clinical trials, it is possible that several other oral/buccal insulin products are already on the market, such as Oral-lyn from Generex and the oral insulin products from Biocon. Since Oral-lyn is buccal insulin, with an effect of more like injectable insulin, which is discussed before, it poses a lesser threat toward oral insulin from Fosse Bio. As for the oral insulin from Biocon, it could be a double-edge sword. On one hand, it can be a strong market competitor, on another hand, launch of two products from two companies together can greatly enhance the confidence of the patient and medical community to accept oral insulin as a credible solution toward diabetes patients.

Fosse Bio has the global right for this drug, and with patents issued both in China and US. They are planning to distribute this oral insulin product through the established network of its parent company, Extrawell Pharmaceutical Holdings Ltd, for domestic market. However, for the international market, Extrawell is actively looking for marketing partners from global pharmaceutical firms. However, with the recent requirements from SFDA for the further clinical trial, the launching of this product will be likely delayed for one or two years upon the approval of SFDA toward further clinical trial data.

As for the national insurance coverage of this drug, most of the domestic insulin products can be covered by national medical insurance system in China, upon negotiation of price and a long application process. Since this oral insulin is discovered by domestic researchers and will be most likely manufactured domestically, it has a big chance to be covered by national medical insurance upon SFDA approval. However, the application is a long process, and the final approval is upon negotiation with the national medical insurance with a low price which can be accepted by the national insurance system. Consequently, if the drug is included into the national list for insurance coverage, the price will have to be negotiated between government and drug manufacturer. In another word, drug price will be partly controlled by the government if the drug manufacturer wants its products included into the national insurance coverage list. Otherwise, the price of the drug can freely defined by the manufacturer according to the market requirements and their market strategy.

Summaries:

1. This oral insulin seems like a good technology, with sounded scientific proof from basic and animal research from a famous university.
2. Initially, the oral insulin from Fosse Bio was expected to be categorized into degree 4 drug, when it was applied by changing delivery process of insulin, while only a small clinical trial is needed for its approval.
3. The valuation of this drug (or the project) was further pushed up by the upcoming Exubera and other insulin drugs developed by big pharmaceutical firms.

4. However, Exubera was withdrawn from the market eventually, and the development of some inhaled insulin stopped as well. All the sudden, the future of this market looks loom and becomes uncertain. Some people now begin to question the valuation of this drug. However, oral intake solves exactly the major issue of toxicity brought by inhaled insulin by taking the drug through digestive track instead of through patients' lung.
5. Inside SFDA, they are in a learning phase of this oral insulin while the regulation becomes tight and inspector becomes more cautious after the new governance took the stage with a more stringent review policy. They now regard the previous clinical trials non-conclusive, though the result is successful according to their previous requirements. They asked for further clinical trial, including a double-blind trial, which is typically required only for new drug studies (SFDA now regard this drug as degree 2 of the new drug development).
6. As for the future of this drug, with the results from the previous clinical trials, it seems to act more like long-acting insulin than injectable regular insulin. Therefore, the market could be bigger than before though more clinical research and marketing will be needed for its launch.

Therefore, there will be additional cost and time required for this further clinical trial. Our estimation in total for this trial and to get the approval from SFDA is about two years and additional USD2 million required. In addition, SFDA required the adjustment of the indication of the oral insulin from replacement of injectable regular insulin to the long-acting insulin to enhance the basal insulin level of the diabetes patients, which will definitely affect the application and market size, hence the value of the new oral insulin from Fosse Bio.

Conclusion

The advanced methods of insulin delivery systems would gradually progress toward physiological insulin replacement and reduce the long-term complications of diabetes mellitus. Thus, a feasible alternative route for insulin delivery is likely to emerge in the future. This new millennium promises a revolutionary change in the delivery of insulin, which is not too far off for billions of sufferers who are reliant on subcutaneous injective administration. The approaches that seem to hold potential must be consolidated and converted to a working protocol. Among the various alternative delivery systems, each have their own set of favorable and unfavorable properties. Some unfavorable aspects have to be circumvented to make this alternative insulin delivery system a reality and make them to reach the market.

By far, although having acceptable results of controlling blood sugar level, inhaled insulin seems facing difficulty in entering the market because of long-term lung safety problem which has influenced the confidence of the players in novel insulin delivery industry. However, several of the candidates keep our confidence high in this high stake market. We keep a cautious view upon the oral insulin system; though we believe it will be the next milestone in the diabetes treatment technology.

(We have reviewed the bases and assumptions used in the valuation of Smart Ascent, and considered such bases and assumptions fair, reasonable and complete)

PKU Medical Investment Co. (PUMIC)
Dr. Adam ZHAO, PhD Dr. Long JIANG, MD

Notes:

1. Dr. Adam Zhao holds a PhD in molecular biology from University of Pittsburgh, School of Medicine, and a Master's Degree of Business Administration (MBA) from University of Chicago, Booth Graduate School of Business. Dr. Zhao has over 10 years of experience, specializes in lifesciences, pharmaceuticals, biotech and other healthcare related areas. Before PKU Medical Investment Co, Dr. Zhao was a Senior Manager at Pfizer in New York, where he was responsible for drug evaluation, product marketing and business development. Dr. Adam Zhao also worked in technical transfer office of University of Pittsburgh, School of Medicine, where he was in charge of technical assessment and commercial evaluation of new technologies.
2. Dr. Long Jiang holds a medical degree from Harbin Medical University and was a practice heart surgeon in People's Hospital, Peking University, School of Medicine. He is also a founder of Starwood International Heart Hospital in Tsingdao and a director for the hospital for over five years. He has over ten years of experience in hospital management, medical device distribution, and pharmaceutical marketing and distribution.

1. RESPONSIBILITY STATEMENT

This circular includes particulars given in compliance with the Listing Rules for the purpose of giving information with regard to the Company. The Directors collectively and individually accept full responsibility for the accuracy of the information contained in this circular and confirm, having made all reasonable enquiries, that to the best of their knowledge and belief there are no other facts the omission of which would make any statement herein misleading.

2. DIRECTORS' INTERESTS AND SHORT POSITIONS IN SHARES, UNDERLYING SHARES AND DEBENTURE

- (a) As at the Latest Practicable Date, the interests and short positions of each Director and the chief executive of the Company in the Shares, underlying Shares or debentures of the Company or any of its associated corporations (within the meaning of Part XV of the SFO) which (a) were required to be notified to the Company and the Stock Exchange pursuant to Divisions 7 and 8 of Part XV of the SFO (including interests and short positions in which he was deemed or taken to have under such provisions of the SFO); or (b) were required pursuant to Section 352 of the SFO to be entered in the register maintained by the Company referred to therein; or (c) were required pursuant to the Model Code for Securities Transactions by Directors of Listed Issuers (the “**Model Code**”) contained in the Listing Rules, to be notified to the Company and the Stock Exchange, were as follows:

Name of Director	Name of company	Capacity	Number and class of securities	Approximate percentage of interests held
Dr. Mao Yu Min	The Company	Interest of controlled corporation (<i>Note 2</i>)	480,000,000 Shares (L)	20.96%
Dr. Xie Yi	The Company	Interest of controlled corporation (<i>Note 2</i>)	480,000,000 Shares (L)	20.96%

Notes:

- (1) The letter “L” represents the Director’s interests in the shares and underlying shares of the Company or its associated corporations.
- (2) Each of JNJ Investments Ltd. (“**JNJ Investments**”) and Fudan Pharmaceutical Limited (“**FPL**”) holds 450,000,000 and 30,000,000 Shares respectively.

The entire issued share capital of JNJ Investments is owned by Biowindow Gene Development (Hong Kong) Limited (“**HK Biowindow**”), the issued share capital of which is owned as to 99% by United Gene Group Ltd., as to 0.99% by United Gene Holdings Limited (聯合基因科技有限公司) (“**United Gene-PRC**”) (a company established in the PRC) and as to 0.01% by Shanghai Biowindow Gene Development Co., Ltd. (“**Shanghai Biowindow**”).

The issued share capital of United Gene Group Ltd. is owned as to 33% by United Gene Holdings Limited (“**United Gene-BVI**”) (a company incorporated in the British Virgin Islands) and as to 33% by Ease Gold Investments Limited. The issued share capital of United Gene-BVI and Ease Gold Investments Limited is wholly owned by Dr. Mao Yu Min and Dr. Xie Yi respectively.

The capital of Shanghai Biowindow is 60% owned by United Gene-PRC, 13.575% owned by Dr. Xie Yi and 13.575% owned by Ms. Sheng Xiao Yu, who is the wife of Dr. Mao Yu Min. The equity capital of United Gene-PRC is beneficially owned as to 33.5% by Dr. Mao Yu Min and as to 33.5% (including 8.5% direct interest and 25% indirectly through his shareholding in Ease Gold Investments Limited) by Dr. Xie Yi.

HK Biowindow owned 80% of the share capital of FPL.

Each of Dr. Mao Yu Min and Dr. Xie Yi is taken to be interested in all the Shares in which each of JNJ Investments and FPL is interested by virtue of the SFO.

- (b) Save as disclosed in paragraph 2(a) above, as at the Latest Practicable Date, none of the Directors or the chief executive of the Company had any interest and short positions in the Shares, underlying Shares and debentures of the Company or any of its associated corporations (within the meaning of Part XV of the SFO) which (a) were required to be notified to the Company and the Stock Exchange pursuant to Divisions 7 and 8 of Part XV of the SFO (including interests and short positions in which he was deemed or taken to have under such provisions of the SFO); or (b) were required pursuant to Section 352 of the SFO to be entered in the register maintained by the Company referred to therein; or (c) were required pursuant to the Model Code contained in the Listing Rules, to be notified to the Company and the Stock Exchange.
- (c) As at the Latest Practicable Date, none of the Directors had any direct or indirect interest in any asset which had been acquired, or disposed of by, or leased to any member of the Group, or was proposed to be acquired, or disposed of by, or leased to any member of the Group since 31 March 2008, the date to which the latest published audited financial statements of the Group were made up.
- (d) As at the Latest Practicable Date, none of the Directors was materially interested, directly or indirectly, in any contract or arrangement entered into by any member of the Group subsisting as at the date of this circular.
- (e) As at the Latest Practicable Date, none of the Directors or their respective associates was interested in any business apart from the business of the Group, which competed or was likely to compete, either directly or indirectly, with that of the Group.

3. SUBSTANTIAL SHAREHOLDERS

- (a) As at the Latest Practicable Date, so far as is known to the Directors, the following persons, other than a director or chief executive of the Company, had an interest or short position in the Shares and underlying Shares which would fall to be disclosed to the Company and the Stock Exchange under the provisions of the Divisions 2 and 3 of Part XV of the SFO, or

were directly or indirectly, interested in 10% or more of the nominal value of any class of share capital carrying rights to vote in all circumstances at general meetings of any other member of the Group:

Name of Shareholder	Number of Shares (Note 1)	Capacity (Note 2)	Approximate percentage of interests held
Ease Gold Investments Limited	480,000,000 Shares (L)	Interest of controlled corporation	20.96%
United Gene – BVI	480,000,000 Shares (L)	Interest of controlled corporation	20.96%
United Gene Group Ltd.	480,000,000 Shares (L)	Interest of controlled corporation	20.96%
HK Biowindow	480,000,000 Shares (L)	Interest of controlled corporation	20.96%
JNJ Investments	450,000,000 Shares (L)	Beneficial owner	19.65%
Mr. Ong Cheng Heang (Note 3)	300,000,000 Shares (L)	Beneficial owner	13.10%

Notes:

- (1) The letter “L” represents the entity’s interests in the Shares.
- (2) Each of JNJ Investments and FPL holds 450,000,000 and 30,000,000 Shares respectively.

The entire issued share capital of JNJ Investments is owned by HK Biowindow, the issued share capital of which is owned as to 99% by United Gene Group Ltd., as to 0.99% by United Gene-PRC and as to 0.01% by Shanghai Biowindow.

The issued share capital of United Gene Group Ltd. is owned as to 33% by United Gene – BVI and as to 33% by Ease Gold Investments Limited. The issued share capital of United Gene-BVI and Ease Gold Investments Limited was wholly owned by Dr. Mao Yu Min and Dr. Xie Yi respectively.

The capital of Shanghai Biowindow is 60% owned by United Gene-PRC, 13.575% owned by Dr. Xie Yi and 13.575% owned by Ms. Sheng Xiao Yu, who is the wife of Dr. Mao Yu Min. The equity capital of United Gene-PRC is beneficially owned as to 33.5% by Dr. Mao Yu Min and as to 33.5% (including 8.5% direct interest and 25% indirectly through his shareholding in Ease Gold Investments Limited) by Dr. Xie Yi.

HK Biowindow owned 80% of the share capital of FPL.

- (3) Mr. Ong Cheng Heang is interested in the 300,000,000 Shares, which are the Consideration Shares to be allotted and issued to him pursuant to the 2007 Agreement.

- (b) As at the Latest Practicable Date, so far as is known to the Directors, the following persons were directly or indirectly, interested in 10% or more of the nominal value of any class of share capital carrying rights to vote in all circumstances at general meetings of any member of the Group (other than the Company):

Name of the company	Name of shareholder	Number of shares/amount of registered capital held	Approximate percentage of interests held
Changchun Extrawell Pharmaceutical Co., Ltd.	吉林省天和對外經濟貿易集團有限公司	RMB9,140,000	18%
Grand Success Management Limited	Charmtex Investments Limited	10,000 shares of US\$1 each	20%
Smart Ascent	Mr. Ong	4,900 shares of HK\$1 each	49%
Fosse Bio	Fordnew Industrial Limited	2,900 shares of HK\$1 each	29%
Welly Surplus	Smart Allied Holdings Limited	29 shares of HK\$1 each	29%
Welly Surplus	Goachieve Holdings Limited	20 shares of HK\$1 each	20%

Save as disclosed in this circular, as at the Latest Practicable Date, so far as is known to the Directors or chief executive of the Company, there was no other person who had an interest or short position in the Shares, underlying Shares and debentures of the Company which would fall to be disclosed to the Company and the Stock Exchange under the provisions of the Divisions 2 and 3 of Part XV of the SFO, or who were directly or indirectly, interested in 10% or more of the nominal value of any class of share capital carrying rights to vote in all circumstances at general meetings of any other member of the Group.

4. DIRECTORS' SERVICE CONTRACTS

As at the Latest Practicable Date, none of the Directors had entered or proposed to enter into a service contract with any member of the Group which is not determinable by the employer within one year without payment of compensation (other than statutory compensation).

5. MATERIAL ADVERSE CHANGES

The Directors are not aware of any material adverse change in the financial or trading position of the Group since 31 March 2008, being the date to which the latest published audited financial statements of the Group were made up.

6. COMPETING INTEREST

As at the Latest Practicable Date, none of the Directors and his associates was interested in any business apart from the business of the Group, which competes or is likely to compete, either directly or indirectly, with that of the Group which would otherwise be required to be disclosed under Rule 8.10 of the Listing Rules if any of such Directors or his associates was a controlling Shareholder.

7. LITIGATION

As at the Latest Practicable Date, none of any member of the Group was engaged in any litigation or arbitration of material importance and no litigation or claims of material importance known to the Directors to be pending or threatened by or against any member of the Group.

8. QUALIFICATIONS AND CONSENTS OF THE EXPERTS

- (a) The following are the qualifications of the experts who have given their reports, opinions or advice which are included in this circular:

Name	Qualification
Somerley	Corporation licensed to carry out business in type 1 (dealing in securities), type 4 (advising on securities), type 6 (advising on corporate finance) and type 9 (asset management) regulated activities under the SFO
RSM Nelson Wheeler	Certified Public Accountants
Castores Magi Asia Limited	Registered Professional Surveyors
PKU Medical Investment Co.	Medical and healthcare-related matters consultants

- (b) None of Somerley, RSM Nelson Wheeler, Castores Magi Asia Limited and PKU Medical Investment Co. has any shareholding, directly or indirectly, in any member of the Group or any right (whether legally enforceable or not) to subscribe for or to nominate persons to subscribe for securities in any member of the Group.
- (c) Each of Somerley, RSM Nelson Wheeler, Castores Magi Asia Limited and PKU Medical Investment Co. has given and has not withdrawn its written consent to the issue of this circular, with copies of its letter and/or reports and the references to its name included in the forms and contexts in which they are respectively included.
- (d) None of Somerley, RSM Nelson Wheeler, Castores Magi Asia Limited and PKU Medical Investment Co. had any direct or indirect interest in any asset which had been acquired, or disposed of by, or leased to any member of the Group, or was proposed to be acquired, or disposed of by, or leased to any member of the Group since 31 March 2008, the date to which the latest published audited financial statements of the Group were made up.

9. MISCELLANEOUS

In the event of inconsistency, the English text of this circular shall prevail over the Chinese text.

10. DOCUMENTS AVAILABLE FOR INSPECTION

Copies of the following documents are available for inspection during normal business hours at the head office and principal place of business of the Company in Hong Kong, Room 3409–10, 34/F, China Resources Building, 26 Harbour Road, Wanchai, Hong Kong, up to and including the date of the SGM:

- (a) the 2004 Agreement;
- (b) the 2007 Agreement;
- (c) the memorandum and bye-laws of the Company;
- (d) the letter from the Independent Board Committee, the text of which is set out on page 22 of this circular;
- (e) the letter from Somerley, the text of which is set out on pages 23 to 51 of this circular;
- (f) the valuation report issued by Castores Magi Asia Limited, the text of which is set out in Appendix I to this circular;
- (g) the report from RSM Nelson Wheeler in relation to the valuation of the Smart Ascent Group, the text of which is set out in Appendix I to this circular;
- (h) the accountants' report of the Smart Ascent Group, the text of which is set out in Appendix II to this circular;
- (i) the market report issued by PKU Medical Investment Co., the text of which is set out in Appendix III to this circular;
- (j) the letters of consent referred to in the section headed "Qualifications and Consents of Experts" in this appendix; and
- (k) this circular.



EXTRAWELL PHARMACEUTICAL HOLDINGS LIMITED

精 優 藥 業 控 股 有 限 公 司 *

(incorporated in Bermuda with limited liability)

(Stock Code: 00858)

NOTICE OF SPECIAL GENERAL MEETING

NOTICE IS HEREBY GIVEN that a special general meeting of Extrawell Pharmaceutical Holdings Limited (the “**Company**”) will be held at Harbour View Room III & IV, 3rd Floor, The Excelsior, Hong Kong, 281 Gloucester Road, Causeway Bay, Hong Kong on Monday, 8 June 2009 at 11:00 a.m. for the purpose of considering and, if thought fit, passing with or without amendments, the following resolution as an ordinary resolution of the Company:

ORDINARY RESOLUTION

“**THAT** the acquisition (the “**2004 Acquisition**”) by Extrawell BVI Limited from Mr. Ong Cheng Heang and Ms. Wu Kiet Ming (collectively, the “**Vendors**”) in August 2004 of an aggregate of 51% interest in the share capital of Smart Ascent Limited pursuant to the acquisition agreement (the “**2004 Agreement**”) dated 3 March 2004 (a copy of which has been produced to the meeting marked “A” and signed by the chairman of the meeting for the purpose of identification) and entered into between the Vendors as vendors and Extrawell BVI Limited as purchaser and the transactions contemplated thereby be and are hereby approved, confirmed and ratified, and any action taken or implemented by the directors of the Company in connection with the 2004 Acquisition prior to the passing of this resolution be and it is hereby approved, confirmed and ratified, and the directors of the Company be and they are hereby authorised to take such steps as they may consider necessary, appropriate, desirable or expedient to implement or give effect to the 2004 Acquisition, the terms of the 2004 Agreement or all transactions contemplated under the 2004 Agreement.”

By order of the Board
Extrawell Pharmaceutical Holdings Limited
Mao Yu Min
Chairman

Hong Kong, 21 May 2009

* For identification purpose only

NOTICE OF SGM

Executive directors:

Dr. Mao Yu Min
Dr. Xie Yi
Dr. Lou Yi
Ms. Wong Sau Kuen

Independent non-executive directors:

Mr. Fang Lin Hu
Mr. Xue Jing Lun
Ms. Jin Song

*Head office and principal place
of business in Hong Kong:*

Room 3409–10, 34/F
China Resources Building
26 Harbour Road
Wanchai
Hong Kong

Notes:

- (1) A member entitled to attend and vote at the meeting convened by the above notice or any adjournment thereof is entitled to appoint one or more than one proxy to attend and, subject to the provisions of the bye-laws of the Company, vote in his stead. A proxy need not be a member of the Company.
- (2) A form of proxy for use at the meeting is enclosed. In order to be valid, the form of proxy must be duly completed and signed in accordance with the instructions printed thereon and deposited together with a power of attorney or other authority, if any, under which it is signed or a notarially certified copy of that power or authority, at the office of the Company's Hong Kong branch share registrar, Tricor Tengis Limited at 26/F, Tesbury Centre, 28 Queen's Road East, Hong Kong no less than 48 hours before the time for holding the meeting or any adjournment thereof.
- (3) Delivery of an instrument appointing a proxy should not preclude a member from attending and voting in person at the above meeting or any adjournment thereof and in such event, the instrument appointing a proxy shall be deemed to be revoked.
- (4) In the case of joint holders of a share, any one of such joint holders may vote, either in person or by proxy, in respect of such share as if he/she/it was solely entitled thereto to. If more than one of such joint holders are present at the above meeting, the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other joint holders. For this purpose, seniority shall be determined by the order in which the names stand in the register of members of the Company in respect of the joint holding.