ASX Announcement
30 October 2020

Invex Provides Development Update

Highlights:

- **Next stage of protocol assistance with EMA submitted; feedback expected late Q4 CY2020**
- **FDA pre-IND meeting request to be made post EMA feedback**
- **Decision on final formulation for human clinical studies in IIH expected Q4 CY2020**
- **Manufacturing agreement to be finalised Q4 CY2020**
- **Presendin™ for clinical studies to be available 1H CY2021**
- **Human pharmacokinetic (PK) study to commence 1H CY2021**
- **Tolerability study to commence 1H CY2021**
- **Commencement of a Phase III trial still expected 1H CY2021**

Invex Therapeutics Ltd (**Invex**, **ASX:IXC,** or **the Company**) a clinical-stage biopharmaceutical company focused on the development and commercialisation of Presendin™ (Exenatide) for neurological conditions relating to raised intracranial pressure, provides below a development update following expert review of the initial regulatory feedback received from both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) on the Company's development plan for Presendin™ in Idiopathic Intracranial Hypertension (IIH).

Regulatory Update

Invex's regulatory strategy has always been based on exploiting the benefits of its Orphan Drug Designation to undertake multiple, iterative, interactions with authorities. In reacting to regulatory authorities' advice, Invex has sought expert advice from regulatory consultants, statisticians and an independent advisory board comprised of clinical experts in both neurology and ophthalmology and Chaired by Invex's Executive Director and Chief Scientific Officer Professor Alex Sinclair.

Having received the first response of authorities in July 2020, Invex submitted a protocol assistance briefing document with a formal response and additional questions to the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) for consideration in October 2020.

Protocol assistance is a special form of scientific advice only available to developers of designated orphan medicines for rare diseases. Exenatide for IIH was granted such Orphan Drug Designation in March 2016. In addition to scientific advice, Invex can receive answers to questions relating to

the criteria for authorisation of an orphan drug. Scientific advice can be sought at any stage of drug development and within any area of development to assist drug developers by providing expert responses to specific questions related to the development of a particular medicine.

The purpose of the follow-up protocol assistance advice by Invex is to receive direct regulatory feedback from CHMP on revisions to the proposed Phase III study design for Invex's proprietary Presendin™ formulation of Exenatide. The Company has sought follow-up advice primarily with the proposed Phase III clinical trial as initial feedback from EMA highlighted the broad acceptability of Invex's pre-clinical package and lead-in human pharmacokinetic study plan.

The Company has sought further advice from CHMP on the acceptability of monthly headache days as a primary endpoint for the planned single pivotal study comparing Presendin™ to placebo at 24 weeks. The Phase II study showed Exenatide conferred a statistically significant and clinically meaningful 7.7 day (37%) reduction in monthly headache versus placebo.[1] Additionally, based on the advice received to date, the Company will no longer consider an open-label extension of 24 weeks plus 4 weeks follow up envisaged with the initial Phase III design[2], which Invex expects will result in a reduction of overall trial duration and cost.

Headache is the predominant morbidity occurring in up to 94% of IIH patients. Despite the potential risk of blindness due to presence of papilloedema (swelling of the optic nerve due to intracranial pressure (ICP) effects), headache has the greatest impact on patient's health related quality of life. Moreover, there is a high rate of repeat hospital admission in IIH, which is driven by headache and reflected in escalating healthcare costs estimated to be £462 million per annum by 2030 in the UK, representing close to a five-fold increase on 2017 levels.

Subject to the follow up feedback obtained by CHMP, the Company's current intention is to submit a Clinical Trial Application (CTA) within selected European countries in the 1H of CY2021 to commence a single pivotal clinical trial for registration of Presendin™ in IIH.

If such a trial is ultimately successful, a single marketing authorisation (MAA) under Invex's orphan drug designation will be made to EMA via the centralised authorisation procedure, which would allow Invex to market and sell Presendin™ throughout the European Union.

<u>FDA Submission to follow CHMP Response to Protocol Assistance</u>

Subject to the feedback from CHMP, the Company intends to then request a Type B / pre-Investigational New Drug Application (IND) meeting with the FDA. Type B meetings typically occur within 60 days of a request being made. The protocol assistance received from CHMP will be an important consideration in formulating the necessary feedback to be sought from the FDA.

Per initial feedback received from the FDA in July 2020[3], Invex intends to submit with its meeting request a complete protocol and statistical analysis plan for Presendin™. The FDA considers the reduction in monthly headache days to be a clinically meaningful endpoint, as is the reduction in the use of acute headache medications.

[1] ASX announcement dated 20 May 2020
[2] ASX Announcement dated 22 May 2020
[3] ASX announcement dated 23 July 2020

The Company believes this strategy optimises the benefit(s) obtained through additional feedback from CHMP to refine the assistance sought with the FDA to more effectively harmonise trial design between Europe and the US.

Reformulation and Manufacturing Update

The Company has been developing several different formulations of Presendin™ for sub-cutaneous delivery to IIH patients. These formulations are the subject of novel patent applications submitted by Invex in Q1 CY2020. The Company successfully completed a series of animal pharmacokinetic (PK) experiments during Q2 and Q3 2020 with its formulation candidates, but a final formulation decision has been delayed due to COVID-19 impacts related to the timely availability of appropriate laboratory testing personnel and facilities. Final formulation selection is a critical determinant in executing a manufacturing agreement for supply of Presendin™.

Accordingly, the decision on the preferred formulation and manufacturing partner for Good Manufacturing Practice (GMP) supply of clinical material will be made in Q4 2020 when it is expected the full set of PK results will be available. Discussions with several potential manufacturers are well-advanced.

Tolerability and Human PK Trial

All formulation excipient(s) in the different formulations have precedence of human exposure via parenteral (non-oral) route and a well-established safety profile in humans and as per initial regulatory advice, Invex does not plan to undertake any additional safety or toxicity studies for Presendin™, other than a local tolerability study.

Invex is required to conduct a local tolerability study of Presendin™ by examining the effect (if any) at the injection site in animals. The timing of this study will be determined by the availability of clinical grade Presendin™, as discussed above. The Company expects to undertake the necessary animal tolerability study in 1H CY2021 (previously Q4 CY2020).

As a reformulation of an existing approved drug, Invex is required to conduct a human Phase I study to investigate the PK and safety of the administration of single and repeated subcutaneous doses of Presendin™. Invex will make a comparison to the approved Exenatide drug product (Byetta®) in healthy volunteers to ensure that the total bioavailable drug does not exceed what is already approved by authorities for Byetta®. This study is expected to commence in 1H CY2021 (previously Q4 CY2020), with results expected during the same period.

Summary & Outlook

The Company has undertaken a significant level of consultation following completion of its Phase II clinical trial in IIH and subsequent initial protocol advice from the EMA and FDA.

Invex anticipates a CTA will be filed to commence a Phase III trial during the 1H CY2021 as planned. The timing of an IND filing with the FDA will be dependent on the regulatory advice received

following a pre-IND meeting request, which will be filed after the Company receives a response to protocol assistance sought from CHMP in Q4 CY2020.

Regulatory interactions are complex and time consuming by nature. These necessary steps are important to allow Invex to develop a well-designed clinical trial, while also ensuring all necessary safety and toxicity parameters are met prior to filing for marketing clearance. Although the Company has experienced some delays in its lead-in development work due to COVID-19, Invex remains committed to its clinical program in 2021.

The Company remains well funded with cash and cash equivalents of $33.9 million as at 30 September 2020.

This release dated 30 October 2020 has been authorised for lodgement to ASX by the Board of Directors of Invex Therapeutics and lodged by Narelle Warren, Company Secretary.

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About Invex Therapeutics Ltd

Invex is a biopharmaceutical company focused on the repurposing of an already approved drug, Exenatide, for efficacious treatment of neurological conditions derived from or involving raised intracranial pressure, such as Idiopathic Intracranial Hypertension (IIH), acute stroke and traumatic brain injury. Invex has trademarked its repurposed Exenatide as Presendin™. www.invextherapeutics.com.

About Idiopathic Intracranial Hypertension (IIH)

IIH features severely raised intracranial pressure which causes disabling daily headaches and can compress the optic nerve, causing permanent vision loss in 25% of those affected. The usual age of onset is 20-30 years, and it is most common in women who are obese. IIH is a rapidly growing orphan indication: its incidence has increased by more than 350% in the last 10 years.

About Exenatide

Exenatide is a small peptide and a synthetic version of the GLP-1 agonist exendin-4, which received approval in the US and Europe for the treatment of type 2 diabetes in 2005 and 2006 respectively. Professor Alexandra Sinclair's research showed that GLP-1 receptors are expressed in the choroid plexus in the brain and that Exenatide can bind to these receptors and reduce secretion of cerebrospinal fluid. Current Exenatide dosage forms are not optimised for IIH.