ASX Announcement

23rd July 2020

Invex Receives Initial FDA and EMA Advice on Presendin™ Development

Key Points:

- EMA indicated a single pivotal study of Presendin™ v placebo would be sufficient to support a filing for regulatory approval in idiopathic intracranial hypertension (IIH) in Europe
- The FDA stated they would need more information to evaluate the Company's proposed design but did guide that two well controlled studies would be required to support registration in the US
- Invex's proposed preclinical and human pharmacokinetic approach was acceptable to both EMA and the FDA
- Invex to optimise the registration strategy for both the EU and US over the coming weeks
- The Company remains committed to commencing a pivotal Phase III trial in 1H CY2021 and remains well funded with current cash reserves of $34 million following a successful capital raise in June 2020
- Invex to host **investor conference call at 9.30am today (AEST)** to discuss regulatory feedback (details attached)

Invex Therapeutics Ltd (ASX: **IXC, Invex** or the **Company**) today announced it has received preliminary scientific advice from both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA), regarding its proposed development plans for Presendin™ in idiopathic intracranial hypertension (IIH). Under the auspices of its Orphan Drug Designation Invex sought scientific advice from both the EMA and FDA so as to reduce the likelihood of major objections regarding the development pathway being raised later in development or when seeking approval. The Company has reviewed the EMA and FDA responses and wishes to update investors on progress.

Consistent with the Company's stated regulatory strategy the Company sought early input from both the EMA and FDA on its proposed regulatory pathway which included the overall design of a Phase III trial (enrolling approximately 240 IIH patients with a proposed primary endpoint of perimetric mean deviation (PMD) at six months)[1]. The aim of seeking scientific engagement in parallel was to obtain the broadest and earliest possible feedback from both regulators to ensure time and resources were not wasted on an approach that ultimately could not provide registration potential.

[1] ASX announcements dated 9 March, 20 May, 22 May 2020

The scientific advice received by the Company has broadly endorsed the Company's approach regarding its preclinical components as well as the first in human pharmacokinetic study and will now move forward with these studies consistent with the Company's previous plans. With respect to the clinical requirements both agencies provided helpful clarification on the Company's proposed endpoints for a registration study, and whilst the EMA confirmed its requirement for a single pivotal study for registration, the FDA indicated that two studies would be required.

Dr Jason Loveridge, Chairman of Invex said "In consultation with our regulatory advisors and global clinical advisory board we devised a harmonised regulatory strategy providing an accelerated route for multiple market entry of Presendin™ in IIH. By going to both EMA and FDA early in our development process we have obtained endorsement from the Committee for Medicinal Products for Human Use (CHMP) for our approach in Europe and guidance for a modified approach in the United States."

Dr Loveridge continued "We now have a clear feedback from CHMP on a registration pathway for Europe, which leaves us with a clear route to market in the EU under our orphan drug designation and access to the majority of our market opportunity given the European Union represents around 60% or A$1 billion of our combined annual addressable US-EU market in IIH[2]."

EMA Response

The CHMP, which is the EMA committee responsible for human medicines, provided the Company with the following important advice:

- One well controlled pivotal study providing compelling evidence of safety and efficacy would be sufficient for filing of a marketing authorisation application (MAA) submission in Europe;
- Recommended the Company consider the difference in intracranial pressure between Presendin™ and placebo measured by lumbar punctures after 6 months as the most objective primary outcome for clinical efficacy, with vision and headache outcomes as secondary endpoints;
- Placebo would be considered an acceptable comparator as there is no medical treatment specifically licensed for this condition and nothing has been shown to be effective;
- The proposed non-clinical package could be sufficiently comprehensive for a future marketing application.

FDA Response

The FDA Division of Ophthalmology provided the Company with the following important advice:

- To evaluate the proposed Phase III trial design in detail the FDA would require a complete protocol and statistical analysis plan;
- If the primary endpoint was Perimetric Mean Deviation (PMD) the FDA would expect to see a clinically meaningful change in visual function in two adequate and well controlled studies;
- The reduction in monthly headache days of moderate to severe headaches is a clinically meaningful endpoint, as is the reduction in the use of acute headache medications;

[2] ASX Announcement dated 9 March 2020

- If the Company decided its proposed primary endpoint for registration should not be an assessment of visual function, then future protocol discussions would be required with the Office of Neurology at the FDA.

Company Next Steps

The Company will now consult with its regulatory advisors and clinical advisory board to consider in depth the guidance it has received from the EMA and FDA. This initial advice from the regulators is only the first step in an ongoing discussion with regulatory bodies in Europe and the US.

Importantly, there is now in place a well-defined regulatory pathway for Europe, while in the US the Company will use its Orphan Drug Designation to seek further regulatory input in the future to further clarify and de-risk the development of Presendin™ in IIH.

The Company remains committed to commencing a registration-directed trial in the 1H of CY2021 as previously announced to the market.

Additionally, the Company expects the following milestones in the second half of CY2020:

- Finalisation of the Presendin™ Phase III design (Q3 2020)
- Finalise supply of GMP Exenatide and Presendin™ manufacturing (Q3 2020)
- Complete animal tolerability study for reformulated Exenatide, known as Presendin™ (Q4 2020)
- Initiate human pharmacokinetic (PK) study for Presendin™ (Q4 2020)

The Company remains well funded with cash reserves of $34 million following the completion of the capital raise in June. Invex expects to lodge the Appendix 4C Quarterly Cash Flow and Activities report on Friday 24th July, which will provide the Company's updated cash position as at 30 June.

Investor Conference Call

Dr Jason Loveridge, Chairman of Invex Therapeutics will host an investor conference call commencing at 9.30am Australian Eastern Standard Time (AEST) today to discuss the regulatory feedback, followed by a question and answer session with investors.

Details of the call are set out below.

In order to pre-register for the conference call, please follow the link below. You will be given a unique pin number to enter when you call, providing immediate access to the event.

https://s1.c-conf.com/diamondpass/10008874-invite.html

An audio dial-in facility has been established for the purposes of the meeting, as set out below. Investors are advised to register for the conference in advance by using the Diamond Pass link above to avoid delays in joining the call directly through the operator. Alternatively, investors can elect to dial-in to the meeting. Please allow up to 5-10 minutes for this process.

Conference ID: **10008874**

Participant Dial-in Numbers:
Australia Toll Free: 1800 908299
Australia Local: +61 2 9007 8048
New Zealand: 0800 452 795
Canada/USA: 1855 624 0077
Hong Kong: 800 968 273
Japan: 006 633 868 000
China: 108 001 401 776
Singapore: 800 101 2702
United Kingdom: 0800 0511 453

This release dated 23rd July has been authorised for lodgement to the ASX by the Board of Directors of Invex Therapeutics and lodged by Narelle Warren, Company Secretary.

ENDS

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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.