ASX / Media Release
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Invex to Launch Phase III Clinical Trial in Q4 CY2021 for Registration of Presendin™ in the EU, UK and Australia

Highlights:

- **Invex to proceed with a single, Phase III clinical trial ("IIH EVOLVE") designed to meet the requirements for market approval of Presendin™ for the treatment of Idiopathic Intracranial Hypertension (IIH) in the European Union (EU), United Kingdom (UK) and Australia**
- **240 IIH patients will be randomised to receive either once weekly sub-cutaneous injections of Presendin™ or placebo across 37 centres in Europe, UK, Australia and the United States (US)**
- **The primary endpoint of IIH EVOLVE will assess the mean difference in Intracranial Pressure (ICP) from baseline at 24 weeks between patients receiving Presendin™ and those on placebo**
- **Secondary endpoints will assess the relative difference in vision (Perimetric Mean Deviation (PMD) and papilloedema) and Monthly Headache Days (MHD) between the two groups over 24 weeks**
- **First IIH EVOLVE Clinical Trial Application (CTA) is expected to be filed in Q4 CY2021**
- **Outcomes from IIH EVOLVE to facilitate future discussions with the US FDA regarding registration of Presendin™ in the United States**
- **EU/UK market opportunity estimated to be circa A$1 billion, growing at 3.4% per annum with no regulatory approved treatments**
- **IIH EVOLVE is currently the only clinical trial evaluating a pharmaceutical intervention in IIH, with the trial design based providing the highest possible likelihood of success**
- **IIH EVOLVE trial fully funded from existing cash reserves of $32 million**

Company to Host Investor Webinar today at 5.00 pm AEDT

Invex Therapeutics Ltd (**Invex**, **ASX:IXC,** or **the Company**) a clinical-stage biopharmaceutical company focused on the development and commercialisation of Presendin™ (once weekly extended-release Exenatide) for neurological conditions relating to raised ICP, today provides an update on the Company's regulatory and clinical strategy for Presendin™ in IIH.

Clinical and Regulatory Strategy

Following multiple interactions with global regulators and consultation with clinical advisory groups, Invex will proceed with a clear, lowest risk approach to bring Presendin™ to market as quickly as possible. The Phase III IIH EVOLVE trial is specifically focused on meeting the requirements for

registration of Presendin™ in the EU, the UK and Australia utilising a trial design based on advice received from the European Medicines Agency (EMA). The integration of a combined study based on EMA and US FDA advice received was determined to be a higher risk approach given the differing feedback received on the preferred primary endpoint. Data from IIH EVOLVE is expected to further inform a subsequent development of Presendin™ for the US market. Accordingly, the Company's regulatory strategy will be sequential in nature, based on geographical region and at lower risk.

The primary endpoint of the trial will evaluate the relative change in ICP, with secondary endpoints assessing: i) the minimal clinically important change (MCIC) in vision, measured by PMD, as established by the Neuro-Ophthalmology Research Disease Investigator Consortium and the IIH Treatment Trial[1,2], and ii) headache, utilising a MCIC in MHDs established in recent registration studies in migraine.[3,4]

Based on the Company's analysis of substantial clinical data in IIH collected from three previous large randomised controlled trials, as well as the Invex Phase II trial, the endpoints in the IIH EVOLVE study have been defined with sufficient statistical power to meet the primary outcome of ICP along with the secondary endpoints of PMD, papilloedema and MHD.

Through an extensive outreach program in the EU, UK, US and Australia, the IIH EVOLVE trial protocol has been validated and endorsed by both IIH key opinion leaders as well as patients and their representative organisations. Invex now intends to dedicate its resources towards the completion of all documentation required to initiate recruitment at sites in the EU, UK, Australia, as well as the US, with the first clinical trial application expected to be submitted in Q4 CY2021. To this end, the Company is actively finalising the key documentation required for the initiation of IIH EVOLVE, incorporating new non-clinical and clinical information for Presendin™ under the terms of Invex' recently executed agreement with Peptron.

The Company will include patients from clinical sites in the US (via an Investigational New Drug Application) in IIH EVOLVE. Most likely, IIH EVOLVE will generate substantial clinical data which the Company will use in future discussions with the FDA regarding registration in the US.

Phase III IIH EVOLVE Clinical Trial Design

The Phase III IIH EVOLVE trial is a randomised, placebo-controlled, double-blind, multi-centre trial that will randomise 240 patients with newly diagnosed IIH to determine the efficacy and safety of Presendin™ versus placebo, administered once weekly. Patients with a confirmed diagnosis of IIH will be randomised on a 1:1 basis to either Presendin™ or placebo for 24 weeks.

Primary Objective - To determine the efficacy of Presendin™ administered subcutaneously once weekly for 24 weeks to patients with IIH, as determined by change in ICP, as measured by lumbar puncture at baseline and at 24 weeks.

Secondary Objectives - To determine the effect of Presendin™ on changes in:

- PMD - as measured by Humphrey Visual Field Analysis,
- Papilloedema - utilising optical coherence tomography to evaluate changes in optic nerve head size and retinal nerve fibre layer thickness, and
- MHD – collected via an electronic patient diary.

The Company intends to open 37 participating centres in Europe, UK, US and Australia and anticipates announcing the overall Lead International Investigator for the study and executing agreements with key service providers before the end of 2021. Completion of the IIH EVOLVE trial will be funded from Invex's existing cash reserves of $32 million as at 30 September 2021 and recruitment is anticipated to take approximately 24 months.

Dr Jason Loveridge, Chairman of Invex Therapeutics commented "The recent collaboration and manufacturing agreement with Peptron has enabled us to proceed with our clinical trial planning, with the first clinical doses available for our Phase III trial in Q4 CY2021. Our aim now is to secure an early market approval for Presendin™ in the EU, UK and Australia, and to use the data from IIH EVOLVE to further inform the interaction with the FDA and define fully the requirements for approval in the United States."

Professor Alexandra Sinclair, Executive Director and Chief Scientific Officer of Invex said "I have been the Principal Investigator on four of the five largest prospective randomised clinical trials in IIH. In my role as the Sponsor Trial Director for IIH EVOLVE, this positions Invex well to deliver the outcomes of this Phase III clinical trial, which will be so important for changing the treatment paradigm for IIH patients. My previous trials have provided a wealth of proprietary clinical information and a unique insight into IIH which Invex has leveraged in designing the IIH EVOLVE trial. By combining this with external expert opinion we have a finalised our Phase III clinical trial, which is both widely endorsed across the IIH community of patients and clinicians and designed to meet regulatory requirements for approval in the EU, UK and Australia."

Investor Webinar Details

Invex will today host an investor/analyst interactive webinar to discuss the regulatory and clinical strategy.

The investor webinar will take place at **5.00pm AEDT today** (6.00am BST (London) time), with the following Invex executives, who will provide an overview of the Strategy followed by a question and answer session with investors:

- Dr Tom Duthy, Executive Director (Host/Moderator)
- Dr Jason Loveridge, Chairman and
- Professor Alex Sinclair, Executive Director and Chief Scientific Officer

Investors are required to register for the Webinar prior to the commencement via Zoom at: https://zoom.us/webinar/register/WN_rfRVjfywQm6Xe8M-y22Fsw

Webinar ID: **985 3315 6472**

As an attendee, investors can ask questions in the Q&A, however, both audio and video functions will be disabled except for the presenters. The Q&A panel will be open when you join. Select 'Q&A' at the bottom of the pane if you wish to ask a question. Type your question in the compose box, and then select Send icon. A question can be asked anonymously, if required.

- ENDS -

This release dated 4 November 2021 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. 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 Presendin™

Presendin™ is a once per week, sub-cutaneous, sustained-release (SR) Exenatide microsphere formulation originally developed by Peptron, Inc. (KOSDAQ: 087010). In September 2021 Invex entered into an exclusive collaboration, manufacturing and supply agreement with Peptron for Presendin™ in IIH for all major markets, with the exception of South Korea.

Exenatide is a small peptide and a synthetic version of the GLP-1 agonist exendin-4, which is currently approved for the treatment of type 2 diabetes. In 2017, Invex received orphan drug designation for Exenatide in IIH from the US Food and Drug Administration and European Medicines Agency.

References

[1] NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee, Wall M, McDermott MP, Kieburtz KD, Corbett JJ, Feldon SE, Friedman DI, Katz DM, Keltner JL, Schron EB, Kupersmith MJ. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. JAMA. 2014;311(16):1641-51.

[2] Bruce BB, Digre KB, McDermott MP, Schron EB, Wall M; NORDIC Idiopathic Intracranial Hypertension Study Group. Quality of life at 6 months in the Idiopathic Intracranial Hypertension Treatment Trial. Neurology. 2016;87(18):1871-1877.

[3] Tepper S, Ashina M, Reuter U et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol. 2017 Jin;16(6):425–434.

[4] Sinclair AJ, Burdon MA, Nightingale PG et al. Low energy diet and intracranial pressure in women with idiopathic intracranial hypertension: Prospective cohort study. BMJ. 2010 Jul 7;341:c2701.