ASX / Media Release
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Invex Successfully Concludes Protocol Assistance with EMA

Highlights:

- **Invex successfully concludes protocol assistance process with EMA**
- **Receipt of further protocol assistance from EMA provides Invex with sufficient regulatory input to complete the design of a single Phase III trial to support market approval for Presendin™ in Europe, subject to meeting safety and efficacy requirements**
- **Invex to focus Phase III trial design around key headache and ICP endpoints, both of which were demonstrated to be positively impacted in the Exenatide Phase II trial**
- **European IIH market estimated at close to $1 billion per annum with no approved therapies on the market**
- **Important design elements of EMA response to be integrated into pre-IND / Type B meeting request package with FDA to be filed in Q1 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, today announces further protocol assistance from the European Medicines Agency (EMA) on the Company's proposed clinical development plan for Presendin™ in Idiopathic Intracranial Hypertension (IIH) has been received and the Company has carefully considered the response and next steps.

The Committee for Medicinal Products for Human Use (CHMP) of the EMA were supportive of a single pivotal Phase III trial comparing Presendin™ to placebo in IIH patients with the acceptability of a reduction in headache days over the trial period, subject to establishing that Presendin™ also reduces Intracranial Pressure (ICP) as a trial outcome measure. This provides Invex with the flexibility to structure a clinical trial design for Presendin™ that achieves both a reduction in headache days and the lowering of ICP. The protocol assistance confirmed CHMP's acceptability of headache days as a logical and relevant trial endpoint, which was one of the key submissions made by Invex, given the importance of headache in the clinical setting.

Additionally, CHMP indicated that measuring the effects of Presendin™ to 12 months would be acceptable to ascertain the maintenance of effect in IIH patients. Invex had previously proposed to CHMP an open-label extension after six months for an additional 24 week period, where all patients would receive Presendin™.

Professor Alex Sinclair, Executive Director and Chief Scientific Officer of Invex said "In my own clinic, which is one of the largest globally for IIH, we frequently witness the devasting effect of headaches on patients' quality of life with headache frequency most strongly correlated to patient morbidity and dysfunction. Managing headache is an essential aspect of patient care and the

consensus treatment guidelines in IIH reflect the importance of headache. Therefore, from a scientific and medical perspective, we are encouraged the CHMP is also supportive of Invex designing its registration study for Presendin™ encompassing headache as one of the key outcome measures alongside a benefit in lowering ICP, which we believe our scientific evidence supports."

The underlying mechanism of action of Exenatide in lowering ICP is well established in the scientific literature and Invex has previously reported the results of Exenatide in a Phase II study of IIH patients, which showed a statistically significant and clinically meaningful reduction in ICP of between 18-21% compared to placebo across all three time points measured. Supporting this primary outcome measure was a 7.7 day (37%) reduction in monthly headache days, which was a statistically significant and clinically meaningful response, and a secondary endpoint of the trial.

Dr Thomas Duthy, Executive Director of Invex commented "We are pleased with the outcomes of the follow-up protocol assistance sought from CHMP. Our regulatory strategy seeks to harmonise our Phase III design such that it meets the requirements of both the EMA and US FDA for registration of Presendin™ in IIH, consistent with our orphan designation and subject to meeting key efficacy and safety endpoints. Our strong financial position with $34 million in cash as at 30 September provides the Company with the financial resources to carefully consider an optimised trial design as we prepare to undertake our pre-submission process with the FDA."

The Company will now carefully consider the feedback received when designing the appropriate Phase III trial to support a single marketing authorisation (MAA) in Europe under Invex's orphan drug designation.

In collaboration with its scientific and regulatory advisors, Invex will also integrate key aspects of the CHMP response when considering the necessary pre-IND / type B meeting request submissions with the US FDA, including the preparation of a complete study protocol and statistical analysis plan, per the request of the FDA in July 2020 following receipt of initial advice.

This approach is consistent with the Company's strategy of having obtained such feedback from the CHMP prior to seeking further protocol assistance with the FDA, through the Division of Neurology. The Company anticipates filing such documentation with the FDA to request a pre-IND meeting in Q1 CY2021.

The Company aims 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.

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This release dated 23 December 2020 has been authorised for lodgement to ASX by the Board of Directors of Invex Therapeutics and lodged by Narelle Warren, Company Secretary.

For more information, please contact:

Company/Investors
Dr Thomas Duthy
Executive Director
tduthy@invextherapeutics.com
+61 402 493 727

Media
Margie Livingston
Ignite Communications
margie@ignitecommunications.com.au
+61 438 661 131

To subscribe to Invex email alerts, please visit www.invextherapeutics.com and follow us on Twitter **@InvexThera_ASX**

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.