ASX Announcement

23rd April 2020

Update on Exenatide Phase II Clinical Trial

Invex Therapeutics Ltd (**Invex**, ASX: **IXC,** or the **Company**) today provides an update on the timing of the upcoming results from the single-centre, randomised, double blind, placebo controlled clinical trial comparing twice per day Exenatide subcutaneous injections against placebo in the treatment of Idiopathic Intracranial Hypertension (IIH) in sixteen female patients.

The Company now anticipates the primary endpoint and exploratory (secondary) endpoint analyses will be completed and available in mid to late May 2020 (previous guidance 2Q 2020).

There is currently no approved drug therapy for the treatment of IIH, which Invex estimates could be a market worth up to A$1.6 billion annually in the United States and Europe[1].

IIH is most common in women (~90%) who are obese and of child bearing age and is characterised by elevated pressure of the fluid that surrounds the brain (cerebrospinal fluid or CSF) causing severe headache and visual loss. If left untreated, permanent vision loss can result. Current treatment interventions in the most severe cases are surgical/device based with high rates of recurrence. IIH is a rapidly growing orphan indication driven by increasing obesity, with annual incidence showing a compound annual growth rate (CAGR) of 5.2% between 2002-2016.

Dr Jason Loveridge, Chairman of Invex said "We are looking forward to the unblinding and analysis of this important clinical trial for patients suffering with IIH. Positive clinical results would help to substantiate our understanding of this disease and provide valuable clinical insights for how the Company designs the planned single Phase III registration study as required under the auspices of our granted orphan drug designations."

Invex has provided additional information on the Phase II clinical[2] and current regulatory initiatives with Exenatide in this release to better enable investors to understand and interpret the clinical information once available and disclosed to the market.

In due course, the Company plans to undertake an investor conference call and webcast with the Lead Investigator of the study, Professor Alexandra Sinclair who is also the Chief Scientific Officer and Executive Director of Invex and the Invex Chairman Dr Jason Loveridge following ASX disclosure.

[1] ASX Announcement – Investor Presentation, dated 9 March 2020

[2] ISRCTN Clinical Trial Registry: http://www.isrctn.com/ISRCTN12678718

Study Design
Single centre, randomised, double blind, placebo controlled clinical trial comparing twice per day Exenatide subcutaneous injections against placebo in the treatment of Idiopathic Intracranial Hypertension (IIH) in sixteen female patients.

Primary Endpoints
The primary endpoints of the study focus on changes in intracranial pressure (ICP) between the Exenatide treatment arm and the placebo as measured via a surgically implanted telemetric ICP sensor. Specifically, the primary endpoints will comprise analysis of the change in ICP between time 0, and - 2.5 hours, 24 hours and at the end of trial (12 weeks). The study was designed with 80% statistical power to see a change in ICP between the two groups with a statistically significant outcome determined at a probability of (p)=0.1 or below.

Exploratory (secondary) Endpoints
In the current Phase II clinical study of Exenatide in IIH patients a number of exploratory endpoints (described below) were investigated for their utility as possible primary endpoints in any subsequent Phase III investigation and so were not powered for statistical significance. As such, a non-significant trend in either measure is all that the Company looking for in order to further refine the design of any subsequent clinical studies, particularly a single Phase III registration study.

Headache
Various headache measures will be assessed at time 0 and at 12 weeks using standardised tests. Headache frequency, headache related quality of life (as measured by the Headache Impact Test (HIT)-6 and SP-36 questionnaires), and headache severity (11 point Verbal Rating Scale) have all been utilised previously in IIH clinical studies.

Vision
A number of vision assessments will be made at time 0 and 12 weeks utilising standard tests for visual acuity (Logarithm of the Minimum Angle of Resolution - LogMAR) and visual field (Humphrey Visual Field) as well as Optical Coherence Tomography (OCT) which is used to assess papilloedema in IIH patients.

Inclusion and Exclusion Criteria
The *Inclusion* Criteria for the study were as follows:

- Female
- Aged 18-60 years old
- Diagnosed with IIH by the modified Dandy criteria
- Active disease (papilloedema Frisen grade greater than 1)
- Significantly raised ICP (greater than 25cm CSF)
- No evidence of venous sinus thrombosis (documented normal MR Venogram of CT Venogram)
- Able to provide informed consent

The *Exclusion* Criteria for the study were as follows:

- Aged less than 18 or older than 60 years
- Pregnant or trying to conceive

- Significant co-morbidity, such that in the opinion of the investigator it would not be in the participant's best interest to participate in the trial
- Addison's or Cushing's disease
- Functioning CSF shunt/stent or optic nerve sheath fenestration
- Currently using GLP-1 agonist or DPP-4 inhibitor
- Surgical contra-indication
- Concomitant therapy with acetazolamide, topiramate or diuretics (this can be discontinued 1 month prior to enrolment)
- Inability to give informed consent e.g. due to cognitive impairment

Owing to the breadth of data, and maintenance of the integrity of the data, some secondary endpoint analyses may not be available until a later date or as part of upcoming conference presentations.

Phase III Registration-Directed Clinical Trial Update

The Company continues to plan for a single registration-directed Phase III study of the re-formulated Exenatide (Presendin™) and anticipates commencing a study in the first half of CY2021.

Invex continues to work with leading clinicians in headache and neuro-ophthalmologists in the design of a Phase III study and has utilised their input in a submission of its preferred design to the FDA and EMA for scientific advice.

As previously announced to the market[3] the indicative Phase III study will be a randomised, double blinded placebo controlled, multi-centre clinical study of ~250 patients randomised 1:1 to receive 1x per day re-formulated Exenatide (Presendin™) versus placebo in IIH patients over 24 weeks of treatment. The primary endpoint will be either a headache measure or visual function; with 90% statistical power. Secondary endpoints are expected to also be powered for significance (80%) and include some Quality of Life Measures designed to support pricing and reimbursement following regulatory clearances, if successful.

Multiple Orphan Drug Designations

Invex has secured orphan drug designation for Extenatide in the United States and Europe, providing seven and ten years market exclusivity, respectively, following market entry. In addition, with an orphan drug designation, Invex is eligible for a number of additional government incentives (both financial and non-financial). For example, in the United States, in addition to market exclusivity, the US Food and Drug Administration (US FDA) will:

- waive the ~US $2.9 million Prescription Drug User Fee Act (PDUFA) application fee paid prior to regulatory review, and
- provide protocol assistance for the design and planning of clinical studies.

[3] ASX Announcement – Investor Presentation, dated 9 March 2020

In Europe, similar incentives exist, with an orphan drug also receiving market authorisation centrally in the European Union (i.e. one application to the European Medicines Agency (EMA), one approval valid in all EU member states).

This release dated 23rd April 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 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.