ASX / Media Release
21 August 2023

Invex to Close IIH EVOLVE Phase III Clinical Trial

Key Points:

- Invex to close the IIH EVOLVE Phase III clinical trial for new patients with immediate effect – completion of wind down / close-out of trial expected in majority by 31 December 2023
- Independent market assessment highlights major future impacts to IIH market opportunity for Presendin™
- Current pricing for GLP-1 receptor agonists (GLP-1RA) make Presendin™ uneconomic in IIH and achieving a reimbursement premium for Presendin™ for Invex reflective of its orphan drug status will be challenging
- Full IIH EVOLVE closure costs to be determined following notification of the Company's intention to close IIH EVOLVE with the trial Contract Research Organisation (CRO) (FY23 CRO cost: $4.5 million)
- Excluding CRO costs to close the trial, Invex has identified approximately $2.0 million[1] in additional non-recurring, trial and staff related expenses based on reported FY23 R&D expense of $7.4 million
- Company to explore strategic options to increase the value of the Company's core intellectual property associated with raised intracranial pressure in neurological disorders
- Invex held cash and cash equivalents of $22.5 million at 30 June 2023

The Company will host an investor conference call today at 12.00pm AEST with Dr Tom Duthy, Executive Director – Details Below

Invex Therapeutics Ltd (**Invex**, **ASX:IXC,** or **the Company**) a biopharmaceutical company focused on the development and commercialisation of Presendin™ (sustained release Exenatide) for neurological conditions relating to raised intracranial pressure (ICP), today provides the results of the independent assessment of the Idiopathic Intracranial Hypertension (IIH) market opportunity for Presendin™ from Clarivate, a global leader in providing trusted insights and analytics, with specialist expertise in biopharma intelligence.

The strategic evaluation of Invex's IIH EVOLVE Phase III clinical trial program investigating Presendin™, a GLP-1RA was initiated in response to the rapidly evolving market uptake of GLP-1RAs for the treatment of obesity with or without co-morbidities such as type II diabetes, along with a significant late-stage pipeline of new obesity agents in both oral and injectable formats expected to enter the market in coming years.

[1] Estimate only: subject to GBP/AUD exchange rate

The link between obesity and IIH is well established. Patients with IIH are typically female, and more than 90% of these sufferers are obese.

Based on the research conducted by Clarivate, including interviews with independent opinion leaders in IIH and reimbursement representatives in key European markets, along with recommendations provided to Invex, the Board has made the decision that the continuation of the trial and the necessary expenditure required to complete recruitment under a revised IIH EVOLVE trial is not viable.

Accordingly, the IIH EVOLVE Phase III trial will immediately stop enrolling patients and activating sites, with an orderly wind down of the trial expected to be completed in the majority by 31 December 2023. As at 15 August 2023 the trial had recruited 14 patients (10 active, 4 completed) across 16 sites globally.

The Company will define the cost of IIH EVOLVE closure upon completion of a cost analysis being performed by Invex's Contract Research Organisation, Premier Research, which will be finalised following formal notification of IIH EVOLVE closure. Total CRO expense for the IIH EVOLVE trial in FY23 was approximately $4.5 million.

With the recent changes to the Board and executive management team, along with other expected reductions in consultants, salaries, manufacturing, and logistical costs associated with supporting activities around IIH EVOLVE, Invex has identified approximately $2.0 million in savings based on the FY23 R&D expense of $7.4 million (representing 27% of total reported FY23 R&D expense), to be progressively realised.

The Company's underlying financial position remains strong. Once the Premier Research close out costs are defined, the Company will be able to quantify its expected cash position resulting from the trial.

Dr Tom Duthy, Executive Director of Invex said "The early closure of IIH EVOLVE was a difficult decision for the Board to make, given the significant time and effort of the Company to commence this trial. Although we remain confident in the ability of Presendin™ to lower ICP and improve the clinical symptoms of IIH relating to headache and vision, the simple fact is that these patients are mostly obese, and weight loss is strongly correlated to improvement in IIH symptoms. It therefore stands to reason that the emerging, unfettered supply of affordable and/or reimbursed therapeutic agents with demonstrated long term clinical utility for weight loss, such as Semaglutide (Ozempic®, Wegovy® and Rybelsus®) along with other GLP-1RAs with dual or triple targeting effects now in late-stage clinical development in the field (including oral formulations) will become a preferred treatment option."

The primary principle of IIH management is weight loss, which is considered the disease modifying intervention of choice according to the 2018 IIH Consensus Treatment Guidelines. Exenatide does not exhibit the same weight loss characteristics as other GLP-1RAs from the IIH Phase II Pressure trial reported in 2020 and therefore could be at material risk of obsolescence or substitution in treating IIH patients if regulatory approval and reimbursement was eventually sought by Invex following a clinical trial.

Dr Duthy continued "As a Board we are elected to maximise value for shareholders. Utilising the majority of our cash holdings attempting to complete a revised IIH EVOLVE clinical trial which will take a number of months to obtain new regulatory/ethics clearances is not warranted in light of the significant structural risks to the IIH market in coming years, identified through this independent review and our own internal analysis. A revised trial would also require further feedback from the European Medicines Agency (EMA)

and US Food and Drug Administration (FDA) prior to commencement. There remains a risk one or both of these regulators may disagree with the new trial design as proposed. We also have concerns of the ability to randomise patients to a placebo for 24 weeks given the increased availability of GLP-1RAs for obesity management and the correlation to IIH. We have mitigated these substantial risks by taking decisive action to close the existing trial, materially reduce our future R&D costs and preserve our cash well into the future. We remain excited by the potential of Presendin™ in other pressure-related neurological disorders not correlated to obesity and where Exenatide has shown to have superior ICP lowering effects versus other GLP-1RAs."

Invex has initiated a process of exploring strategic options to enhance the value of the Company's core intellectual property associated with raised ICP in neurological indications including traumatic brain injury (TBI), hydrocephalus and meningitis. Invex expects to secure additional patents in the US and Europe for Exenatide in CY2023 and as previously indicated, expects to secure Orphan Drug Designation for Exenatide in TBI from the US FDA, also in CY2023. Invex received an ODD in TBI for Exenatide from the EMA in June 2023.

The Company continues to develop plans for a proof-of-concept Phase II clinical trial in moderate to severe TBI with Exenatide, which will examine ICP lowering effects within a hospital setting. Further analysis on appropriate dosing regimens and route of administration within this setting remains ongoing.

Investor Conference Call

The Company will host an investor conference call at 12.00pm AEST today with Dr Thomas Duthy, Executive Director.

Details of the call are set out below.

In order to pre-register for the conference call and avoid a queue when calling, please follow the link below. You will be given a unique pin number to enter when you call which will bypass the operator and give you immediate access to the event.

https://s1.c-conf.com/diamondpass/10033160-38uav9.html

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This release dated 21 August 2023 has been authorised for lodgement to ASX by the Board of Directors of Invex Therapeutics.

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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.