ASX / Media Release
10 July 2023

June Quarterly Activities Report & Appendix 4C

Invex Therapeutics Ltd (**Invex**, **ASX:IXC,** or **the Company**) a clinical-stage biopharmaceutical company focused on the development and commercialisation of Presendin™ (sustained release Exenatide) for neurological conditions relating to raised intracranial pressure, today provides an operational and corporate update to accompany its Appendix 4C cash flow statement for the quarter ended 30 June 2023 (Q4 FY23).

Operational Update

IIH EVOLVE Phase III Clinical Trial

For the majority of the quarter, Invex continued to progress site activations and secure additional regulatory approvals to expand the global footprint for the IIH EVOLVE Phase III clinical trial in Idiopathic Intracranial Hypertension (IIH) patients.

On 20 April 2023, the Company the Central Ethics Committee (CEC) and State of Israel Ministry of Health for the IIH EVOLVE clinical trial in Israel. On 21 April 2023, Invex received approval from the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) in France for IIH EVOLVE along with an approved application to the Ethics Committee CPP (Comité de Protection des Personnes). CPP clearance is also required prior to the commencement of a clinical trial in France.

On 28 June 2023, Invex provided an update to the market following a comprehensive review of the reasons behind the slower than expected patient enrolment into the IIH EVOLVE Phase III clinical trial, which commenced in Q4 CY2022.

As of 26 June 2023, the Company had enrolled 13 patients into the IIH EVOLVE trial with a total of 12 sites activated out of the target sites of 40 globally, behind expectations. The Company noted a high number of patients who had been screened (n=25) had failed to be enrolled and over 50 additional IIH patients had been pre-screened and not progressed to screening.

The main factors negatively impacting enrolment were a Perimetric Mean Deviation (PMD) score outside of the inclusion criteria in approximately 60% of IIH patients screened and the majority of pre-screen patients having a diagnostic lumbar puncture to assess their intracranial pressure (ICP) falling outside of the 4 week period immediately prior to formal screening.

In light of the recruitment rate and site activations described above, Invex elected to withdraw guidance relating to the expected recruitment of the IIH EVOLVE trial, which was anticipated at take approximately 24 months from commencement of patient recruitment in Q4 CY2022.

The Board, having consulted extensively with its regulatory and clinical experts, decided to significantly amend the current protocol for the IIH EVOLVE trial and Invex will need to seek the requisite authorities' feedback and ethics committee approvals for a revised protocol.

The primary endpoint will remain unchanged, with Invex assessing the change in intracranial pressure (ICP) from baseline at 24 weeks in the Presendin™ arm versus placebo in newly diagnosed IIH patients who have received a diagnostic lumbar puncture within 6 months of enrolment into the trial (previously 4 weeks). The protocol changes will focus on reordering of the secondary endpoints by replacing PMD as the key secondary endpoint with the more robust Quality of Life Short form 36 (SF-36) Physical component score (PCS).

Independent Assessment – IIH Market Opportunity

On 28 June 2023 the Company announced it had engaged a specialised global healthcare intelligence group to undertake an analysis on the potential future risks to the addressable market for Presendin™ for IIH. This independent assessment was initiated following evidence of the growing use of approved GLP-1 receptor agonists (GLP-1RA) for obesity management, specifically semaglutide, currently sold under the brand names Ozempic®, Wegovy® and Rybelsus®.

Although these drugs have not been impacting recruitment of the IIH EVOLVE clinical trial, due to supply constraints of the approved GLP-1RAs in Europe, this is expected to normalise over time as capacity grows and supply increases. The link between obesity and IIH is well established. Patients with IIH are typically female, and more than 90% of these sufferers are obese. Invex considers the use of these agents in the management of obesity particularly as a key potential future risk to the acceptability of Presendin™ as an orphan treatment in IIH noting this link. Weight loss is considered an effective treatment option for IIH sufferers as it lowers ICP. However, sustainable weight loss is challenging in IIH and across the obesity spectrum.

Following receipt of the report, the Board will be in a position to fully assess the market opportunity for Presendin™ in IIH in light of these new GLP-1RAs including Ozempic® and Wegovy®, their pricing structures and clinician attitudes to prescribing them to treat the obesity associated with IIH.

Orphan Drug Designation in Europe for Exenatide in Moderate to Severe Traumatic Brain Injury

On 23 June 2023, Invex announced the granting of orphan drug designation (ODD) from the European Medicines Agency (EMA) for Exenatide in the treatment of moderate to severe Traumatic Brain Injury (TBI). This is the second ODD for Exenatide in Europe, with Invex receiving an ODD for Idiopathic Intracranial Hypertension (IIH) in 2017, alongside an ODD from the US Food and Drug Administration (FDA), also for IIH.

The EMA provides a range of incentives in the European Union (EU) for medicines that have been granted an orphan designation, including ten years market exclusivity from the date of approval,

clinical trial protocol assistance, access to the centralised authorisation procedure in Europe, and certain fee reductions.

Overall, 57,000 TBI-related deaths and 1.5 million hospitalisations occur every year in the European Union.[i] Management of intracranial pressure (ICP) elevation is considered critical in patients with moderate to severe TBI, however, at present, there are no EMA or FDA approved therapies specifically for the treatment of intracranial hypertension in this patient population.

Corporate Update

Financial Summary and Analysis

The Company closed the quarter in a continued strong financial position with cash and cash equivalents of $22.5 million (Q3 FY23: $23.8 million), with overall cash outflows for the quarter of $1.4 million (Q3 FY23: $1.6 million).

Cash outflows from operating expenditure included:

- Research & Development expenditure for the quarter of $1.2 million (versus $1.2 million in Q3 FY23) reflected costs associated with the Company's contract research organisation managing the Phase III trial, along with clinical and regulatory consultants, and intellectual property costs related to Invex's patent and trademark portfolio. In addition, the Company incurred costs associated with direct R&D staff of $0.22 million (versus $0.21 million in Q3 FY23).

- Administration and corporate costs of $0.19 million (versus $0.19 million in Q3 FY23) include compliance costs associated with an ASX listed company, Director's fees, audit and legal costs.

- Interest received on cash deposits held of $0.23 million (versus $0.22 million in Q3 FY23), which offset the Company's administration and corporate costs for the quarter.

Aggregate amounts paid to related parties of the Company and their associates included in the above costs were $0.25 million for the quarter (versus $0.24 million in Q3 FY23).

Outlook

The IIH EVOLVE trial has been re-designed to accelerate patient recruitment. Although the changes are expected to be cash neutral relative to the original design, to re-start the trial under the revised protocol is expected to take a number of months as the Company seeks the requisite regulatory and ethics committee approvals.

In parallel, the Company awaits the outcome of the market assessment in IIH in mid Q3 CY2023, which will assist the Board in determining whether to continue with the revised protocol change for the IIH EVOLVE Phase III clinical trial.

The Company has filed an additional ODD for the US Market for moderate to severe TBI, which if granted in 2H CY2023 will provide seven years market exclusivity for Exenatide, certain tax credits

and a waiver from the Prescription Drug User Fee Act (PDUFA) fees, which were approximately US$3.1 million in 2022. A proof of concept clinical trial for Exenatide to lower ICP in moderate to severe TBI is under consideration.

Post Quarterly Events

Director Resignations and Appointment of Non-Executive Chairman

On 3 July 2023, Invex announced the resignations of Dr Jason Loveridge, Non-Executive Chairman and Professor Alexandra Sinclair, Executive Director and Chief Scientific Officer, effective 10 July 2023.

The resignations of Dr Loveridge and Professor Sinclair was in response to discussions with major shareholders who indicated to the Company that, following the ASX release on 28 June 2023, they no longer supported their positions as Directors of the Company. Consequently, both Directors felt it was in the best interests of all shareholders to tender their resignations.

Dr Loveridge has been Chairman of Invex since March 2019 and Professor Sinclair an Executive Director since June 2019. Both have made considerable contributions to the Company, including an IPO on ASX and material development of the Company's therapeutic assets. Mr David McAuliffe, current Invex Non-Executive Director, was appointed the Interim Non-Executive Chairman of the Company, effective 10 July 2023.

The resignations of Dr Loveridge and Professor Sinclair, who both hold Director roles with Invex and are engaged by the Company, will not impact current IIH EVOLVE Phase III initiatives, with the Company's management team and contract research organisation, Premier Research Group plc overseeing the trial, alongside the Company's Trial Steering Committee comprising six global key opinion leaders in IIH. Professor Sinclair and Dr Loveridge will cease their engagement with the Company, consistent with their contractual commitments in the months ahead.

- ENDS -

This release dated 10 July 2023 has been authorised for lodgement to ASX by the Board of Directors of Invex Therapeutics.

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. 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.

[i] www.centre-tbi.eu

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity	
Invex Therapeutics Ltd	

ABN	Quarter ended ("current quarter")
29 632 145 334	30 June 2023

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(1,172)	(5,409)
	(b) product manufacturing and operating costs	-	(707)
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs – R&D	(220)	(904)
	(f) administration and corporate costs	(187)	(1,009)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	229	797
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	447
1.8	Other – (D&O insurance)	-	(84)
1.9	**Net cash (used in) operating activities**	**(1,350)**	**(6,869)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
	(f) other non-current assets	-	-
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**-**	**-**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other.	-	-
3.10	**Net cash from / (used in) financing activities**	**-**	**-**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	23,820	29,339
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,350)	(6,869)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	-
4.5	Effect of movement in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of period**	**22,470**	**22,470**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	420	770
5.2	Call deposits	22,050	23,050
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**22,470**	**23,820**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	252
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments

Relates to salaries, consulting and fees paid to Directors. Payments of $36,250 for company secretarial and financial services to Concept Biotech of which Mr McAuliffe is a director and shareholder are included.

7.	**Financing facilities** *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-

7.5	**Unused financing facilities available at quarter end**	-

7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (Item 1.9)	(1,350)
8.2	Cash and cash equivalents at quarter end (Item 4.6)	22,470
8.3	Unused finance facilities available at quarter end (Item 7.5)	-
8.4	Total available funding (Item 8.2 + Item 8.3)	22,470
8.5	**Estimated quarters of funding available (Item 8.4 divided by Item 8.1)**	17

8.6 If Item 8.5 is less than 2 quarters, please provide answers to the following questions:

1. Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer:

2. Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer:

3. Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer:

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

Date: 10 July 2023

Authorised by: Narelle Warren
(On behalf of the Board of Directors)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.