

## Transforming life for people living with Parkinson's

Q2 2023

Gunnar Olsson, CEO Nicholas Waters, EVP and Head of R&D Viktor Siewertz, CFO



### Disclaimer

This document, "IRLAB Therapeutics" (the "Presentation"), has been prepared by IRLAB Therapeutics AB (publ) ("IRLAB") and is provided for informational purposes only.

All information in this Presentation has been compiled in good faith by IRLAB. Neither IRLAB nor any of its directors, employees, affiliates or representatives make any representation or warranty, expressed or implied, as to the accuracy, reliability or completeness of any of the information or projections in the Presentation, or any other written or oral communication transmitted or made available at any time. IRLAB expressly disclaims any and all liability relating to or resulting from the use of such information or communication. The information contained in this Presentation is subject to change, completion or amendment without notice.

Neither this Presentation nor its delivery to any person shall constitute an offer to license, sell or enter into any transaction or commercial agreement. This Presentation does not constitute advice or a recommendation regarding any securities and is not an offer to sell or a solicitation to buy any securities.

Recipients shall be aware of the fact that IRLAB's shares are listed at Nasdaq Stockholm Main Market.



### Today's agenda





## **Operational highlights in the second quarter**

- Mesdopetam
  - In May a discussion was initiated with Ipsen to outline the best way forward for mesdopetam towards registration and make it available to people living with Parkinson's disease
- IRL757 and IRL942
  - In May, IRLAB and the McQuade Center for Strategic Research and Development (MSRD/Otsuka) made an agreement that gives MSRD an exclusive right to evaluate IRLAB's neuropsychiatric programs IRL757 and IRL942. This, to investigate if IRLAB and MSRD can agree to enter a collaboration to develop the compounds through PoC
- Pirepemat
  - End of May, IRLAB announced that all 38 clinics are activated and recruiting patients in the Phase IIb study with pirepemat



## **Operational highlights in the second quarter**

- ISP
  - On June 13–16, IRLAB participated with a presentation at the scientific conference XIV Triennial Meeting of the International Basal Ganglia Society (IBAGS) held in Stockholm
- AGM
  - On June 20, the company's annual general meeting was held where, among other things, three new members were elected to the board Veronica Wallin, Christer Nordstedt and Daniel Johnsson.
- Investor meetings
  - IRLAB presented at several national investor conferences during the period and has ongoing discussions with potential national and international investors to provide updates on the company. Conferences were arranged by ABGSC and Redeye. Recordings are available on IRLAB's website, irlab.se.



## **Operational events after end of period**

#### • Pirepemat

In mid-July the independent safety and data monitoring board, DSMB, gave a unanimous
recommendation to continue the ongoing Phase IIb study with pirepemat in accordance with the
approved study protocol following the first pre-planned data review. The review included the first 25
patients that have completed the treatment phase in the study.

#### • ISP

• IRLAB participated in an international competition focusing on applying Machine Learning (ML) to describe animal behaviour – Behavioural Representation Learning Competition. The competition was arranged by a consortium of machine learning and neuroscience researchers at Northwestern and Caltech Universities. IRLAB was awarded 2nd place in the competition illustrating that IRLAB is in the absolute forefront in the application of ML in its discovery and drug development. An article describing the results was published during the period at the Fortieth International Conference on Machine Learning, July 23, Honolulu, USA. <a href="https://proceedings.mlr.press/v202/sun23g.html">https://proceedings.mlr.press/v202/sun23g.html</a> MABe22: A Multi-Species Multi-Task Benchmark for Learned Representations of Behavior



## **Operational events after end of period**

#### • Mesdopetam

- On August 21, the ownership and rights to the Phase III-ready mesdopetam project was secured to IRLAB. IRLAB now controls the continued clinical development and commercialization
- On August 22, IRLAB gave an update on the mesdopetam project, which included sharing of additional information on the results of mesdopetam's Phase IIb clinical trial in PD-LIDs and the Phase III preparatory Phase I studies conducted by Ipsen. The results show that mesdopetam has a dose-dependent anti-dyskinetic and anti-parkinsonian effect in combination with a tolerability and safety profile on par with placebo, giving mesdopetam a unique position.
- Next step for mesdopetam is an end-of-Phase 2 meeting with the FDA to define the phase III program



Q2 update

## Financial highlights in the second quarter

Net revenue SEK 6.9m (SEK 23.4m)
Total operating expenses SEK 51.7m (SEK 50.6m)
Operating result SEK -44.9m (SEK -27.0m)
Cash flow from operating activities: SEK -52.8m (SEK -44.0m)
Cash and cash equivalents at the end of the period: SEK 156.4m (SEK 322.6m)
Total number of registered shares: 51 868 406 (51 748 406)

Figures in brackets = same period last year, unless otherwise stated



### IRLAB – a world-leading portfolio to improve Parkinson's treatments

| Pioneering<br>biology & ISP   | Focused strategy  | Validated business<br>model based on clinical<br>proof-of-concept                                     | Broad & Solid<br>portfolio   | Organization<br>positioned for<br>success                                    |
|---|---|---|--|--|
| Deep profound<br>understanding of<br>Parkinson's. Team<br>from Nobel laurate<br>Prof. Arvid<br>Carlsson's<br>research group | Discover and<br>develop<br>treatments for PD<br>patients<br>throughout their<br>disease journey | From discovery<br>through Phase I<br>and Phase II to<br>Phase III ready<br>projects and<br>dealmaking | Five unique drug<br>candidates each<br>with blockbuster<br>potential<br>generated by our<br>disruptive ISP<br>platform | Experienced<br>international<br>organization.<br>Listed Nasdaq<br>Stockholm. |



## Parkinson's disease

#### Loss of >50% cells in the brain that produce dopamine

Dopamine is one of the most important signaling substances in the brain. Controlling emotions, thoughts and movements (motor functions)

Why does it happen?

Why is that important?

What happens?

Age is the most important factor. Environmental and genetic factors involved.

| Cardinal symptoms                                 | How do you tell?                         | Current treatment  |  |  |  |  |
|---|--|--|--|--|--|--|
| Tremor  | 〉"Shaking"                               | Levodopa (in combination with agonists, COMTinhibitors and MAO-B inhibitors) |  |  |  |  |
| BradykinesiaSlowness of movingIRigidityStiffnessI |  | Levodopa (in combination with agonists, COMTinhibitors and MAO-B inhibitors) |  |  |  |  |
|   |  | Levodopa (in combination with agonists, COMTinhibitors and MAO-B inhibitors) |  |  |  |  |
| Postural instability                              | $\rangle$ Trouble with balance and falls | No available treatment   |  |  |  |  |
| Other symptoms                                    | Motor: Facial masking                    | , dystonia, drooling etc.  |  |  |  |  |

Non-motor: Hallucinations, apathy, dementia, problems with speech and swallowing

#### Parkinson's disease is chronic and progressive. It is lifelong and worsens over time.



# The most bothersome symptoms according to people with Parkinson's What bothers people with Parkinson's of the second symptoms according to the second symptoms accord

Most frequent bothersome symptoms

- Balance/instability
- Hallmark symptoms
  - Tremor
  - Rigidity
  - bradykinesia
- Cognition and
- Mood

#### Align with areas addressed by IRLAB

What bothers people with Parkinson's disease the most ? Self-reported, n=25 000 (the Fox Insight project, Michael J. Fox Foundation)



SYMPTOMS: Motor ~50%, Non-Motor ~50% of symptom terms

Parkinson's and **IRLAB's solutions** 

## **IRLAB** to address top priorities for management of Parkinson's

Parkinson's is one of the fastest growing **CNS** disorders

2015

6.2

IRLAB



The burden of society from PD in the US alone translates to \$51,800 per year per patient with Parkinson<sup>1</sup>

> References: 1. Yang, G. et al. (2017). Report: Economic Burden and Future Impact of Parkinson's Disease. Lewin Group.; 2. Deane KHO, et al. Priority setting partnership to identify the top 10 research priorities for the management of Parkinson's disease, BMJ Open 2014;4:e006434. doi:10.1136/bmjopen-2014-006434

# Pipeline generated with our unique proprietary drug discovery platform – ISP

### ISP: a new level for drug discovery

- Advanced systems biology technology to discover new candidate drugs (CD)
  - First-in-class drugs
  - Generates strong IP
  - Identifies use area with largest potential for the CD
  - **Gives higher probability** to reach late clinical development compared to industry standard



ISP: effect spectra for CNS drugs



## **Development portfolio transforming** treatment of people living with Parkinson's

|                        |  | Discovery Pred          | clinical Phase I | Phase IIa | Phase IIb | Phase III          | Next major event                                    |  |  |  |
|------------------------|--|-------------------------|------------------|-----------|-----------|--------------------|---|--|--|--|
| Mesdopetam<br>(IRL790) | Parkinson's disease levodopa-<br>induced dyskinesia (PD-LIDs)<br>D3 antagonist |                         |                  |           |           | Phase III<br>ready | End-of-Phase 2     meeting with FDA                 |  |  |  |
|                        | <b>Parkinson's disease Psychosis</b><br>D3 antagonist                          | Phase I III             |                  |           |           |                    |   |  |  |  |
| Pirepemat              | <b>Parkinson's disease impaired<br/>balance and falls</b><br>PFC enhancer      |                         |                  |           | P         | hase IIb           | <b>H1 2024:</b><br>Top-line data<br>Phase IIb study |  |  |  |
| (IRL752)               | <b>Parkinson's disease Dementia</b><br>PFC enhancer                            |                         |                  |           | Phase IIa |                    |   |  |  |  |
| IRL757*                | Apathy in neurology  |                         | Preclinical      |           |           |                    | <b>YE 2023:</b><br>Phase I ready                    |  |  |  |
| IRL942*                | Cognitive impairment in neurology  |                         | Preclinical      |           |           |                    | H1 2024:<br>Phase I ready                           |  |  |  |
| IRL1117                | Parkinson's disease<br>treatment   |                         | Preclinical      |           |           |                    | <b>2024:</b><br>Phase I ready                       |  |  |  |
|                        | * Under evaluation under exclusivity   | by MSRD, an Otsuka comr | banv.            |           |           |                    | 14  |  |  |  |

#### Portfolio









References: Based on Kalia, LV. and Lang, AE. Lancet 2015;386-912.

IRLAB





## World-leading portfolio to improve the treatment of Parkinson's





## Mesdopetam (IRL790) (mes\_dop\_e\_tam)

- Mesdopetam counteracts levodopa-induced dyskinesias (PD-LIDs) by a novel mechanism inhibiting dopamine D3 receptors
- Potential treatment, and prevention, of psychosis in Parkinson's (PD-P)



## Mesdopetam - growing body of clinical evidence supporting a novel treatment of dyskinesia in PD

Clinical studies of mesdopetam



Mesdopetam

## Mesdopetam - Phase IIb study conclusions

- Consistent dose-response and clinically meaningful anti-dyskinetic efficacy
  - Improvement in UDysRS
  - Improvement in "good ON"-time
- Consistent dose-response pattern in reduction in OFF-time, i.e., anti-parkinsonian efficacy
- No untoward effects on normal motor functions or PD symptoms, i.e., no increase of Parkinsonism
- Safety and tolerability profile on par with placebo at all doses
- Predictable plasma exposure linear and dosedependent
- Dose selection for Phase III achieved (7.5 mg b.i.d.)



Comprehensive Phase IIb data presented at MDS Congress, Aug 27-31, 2023

**Abstract Title:** Results from IRL790C005 – A Randomized, Double-Blind, Placebo-Controlled Phase IIb Study Evaluating the Efficacy of Mesdopetam on Daily On-Time without Troublesome Dyskinesia in Patients with Parkinson's Disease

## Mesdopetam - Phase I studies were successfully completed and showed favorable results

Phase III preparation

#### 1. Pharmacokinetics (PK) in Asians and Non-Asians

• PK profile for mesdopetam similar in the different populations

#### 2. Drug-Drug Interaction PK study

- Low risk of drug-drug interactions
- Suggests neither additional clinical drug-drug interaction studies nor restrictions on future patient enrolment would be required in future clinical studies.

#### 3. Mass balance study to evaluate elimination of mesdopetam in humans

• No signs of risk for drug accumulation of in the body

#### Implications of the results

- Predictable PK with low degree of variability
- Anticipated simple and uniform dosing, i.e., low risk of dosing errors



### Mesdopetam - Next steps

Prepare for an end-of-Phase 2 meeting with the FDA

Prepare briefing book in collaboration with regulatory and clinical advisors, as well as support from Ipsen, to define Phase III program

Capitalize on options for financing of Phase III







- Improve balance and reduce falls in Parkinson's (PD-Falls)
- Ongoing randomized, placebo-controlled Phase IIb clinical trial



Pirepemat

## Pirepemat - in development for improvement of balance and reduce falls in Parkinson's

- 45 % of individuals with Parkinson fall recurrently
- Cost of a fall injury approx. 30 000 USD in patients > 65 years
- There is no available treatment despite the large unmet need

#### Status

- Study start of Fas IIb Q1 2022
- All clinical centers activated May 2023
  - Centers in France, Polen, Spain, Sweden, Germany and the Netherlands
- Completion of patient recruitment aimed for end 2023
- Top-line resultatas estimated in H1 2024





## Pirepemat - A first-in-class treatment for impaired balance and reduction of falls

IRLAB

| Mechanism of Action | • <b>Combines antagonism at 5HT7 and alpha-2 receptors</b> leading to highly specific activation of frontal cortex NA and DA  | Volume 374 Number 3 September 2020 ISSN 1521-0103  |
|---------------------|---|--|
| Tolerability        | <ul> <li>Well tolerated in clinical studies</li> <li>Dose range defined</li> </ul>  | PHARMACOLOGY<br>And Experimental Therapeutics  |
| Efficacy            | • <b>Pirepemat shows promising improvements</b> of balance and has potential to reduce falls in Parkinson's by 50%  | Chemical structure and <i>in vitro</i> profile of IRL752<br>30µM<br>25µM<br>25µM<br>15µM<br>5HT7A<br>5HT7A<br>5Gg-1R<br>5ERT             |
| Regulatory          | <ul> <li>Ongoing Phase IIb program developed with regulatory agencies, scientific advisors and regulatory experts</li> <li>EU regulatory agencies: Study and ethical approvals granted; study ongoing.</li> <li>FDA advice to frontload the development plan with additional DMPK and in vitro mechanism studies. These studies are now successfully completed</li> </ul> | Sum<br>Sum<br>MOR<br>MOR<br>MOR<br>MOR<br>Sum<br>MOR<br>Sum<br>MOR<br>Sum<br>Sum<br>Sum<br>Sum<br>Sum<br>Sum<br>Sum<br>Sum<br>Sum<br>Sum |
| Potential           | <ul> <li>About 50% of patients with Parkinson's fall (Hoehn&amp;Yahr stage ≥ 3)</li> <li>Health economic data show cost of falls are very high</li> </ul>   | A Publication of the American Society for<br>Pharmacology and Experimental Therapeutics  |
| Validation          | <ul> <li>WHO-INN proposes new INN, pirepemat (generic name) representing a new CNS compound class = first-in-class</li> <li>Studies published in highly ranked scientific journals</li> </ul>   | About the cover: Pirepemat<br>featured on the cover of<br>the Sep 2020 issue of JPET   |

29

## Pirepemat: Growing body of clinical evidence supporting potential as treatment of falls in Parkinson's

#### **Clinical studies of pirepemat**



## Ongoing Phase IIb study evaluating efficacy of pirepemat on falls frequency in Parkinson's patients

#### Inclusion criteria

- Parkinson's patients (55-85 yrs) with mild cognitive impairment
- Recurrent falls during the past 3 months and at least 2 falls during the past 4 weeks before baseline

#### **Objectives**

- Establish dose for phase III
- Evaluate the effects of pirepemat on falls frequency, cognitive functions, neuropsychiatric EPs and motor function
- Safety and tolerability

AR



#### Top-line data expected H1-24

Regulatory and EC approvals in participating EU countries: France, Germany, Poland, Spain & Sweden. Ongoing process to start up sites in the Netherlands



## **Preclinical projects**

- IRL757 drug candidate
- IRL942 drug candidate
- IRL1117 drug candidate



### **Preclinical projects**

| IRL757<br>Treat apathy in neurology   | IRL942<br>Restore cognitive function  | <b>IRL1117</b><br>Once-daily treatment of<br>Parkinson's   |
|---|---|--|
| Treatment for apathy<br>Loss of initiative, interest and<br>emotional expression/<br>responsiveness | Improvement of cognitive<br>function<br>Memory, perception, attention,<br>reasoning, problem solving and<br>decision-making | Once-daily treatment of<br>Parkinson's (tremor, rigidity,<br>bradykinesia) without<br>troublesome complications<br>-> Next generation Parkinson's<br>treatment |
| Status: IND-enabling studies;<br>Phase I ready YE 2023  | Status: IND-enabling studies;<br>Phase I ready H1 2024  | Status: Preclinical development  |



# IRL757 is aimed at the huge untreated problem with apathy

#### Huge unmet medical need

- Over 10 million US and EU citizens may be affected by apathy
- Apathy occurs in 20-70% in people with PD and In 20-90% of people with AD and other CNS disorders

#### Pathophysiological background

- Disruption of frontal-subcortical neurocircuits are implicated in apathy\*
- IRL757 has a unique ability to **increase neuronal activity** in frontal-subcortical neurocircuits
- Potential for both symptomatic relief and disease modification

#### Apathy

Loss of initiative, interest and emotional expression/ responsiveness, often found in people with dementia.

**Preclinical &** 

research projects





# IRL942 to improve cognitive function in PD and other neurological indications

#### Unmet need among a large population

- 12 % of adults aged 65 years or more experience cognitive decline (CDC)
- Studies demonstrate a high cumulative risk of **dementia** in people with PD. Point prevalence **is 25–30%.**
- Among PD patients without dementia, approximately 25–30% have mild cognitive impairment (MCI), which is evident at the time of diagnosis in 10–20% of patients

IRL942 shows a **unique ability** to activate frontal circuits and **improve cognitive function in preclinical models** 

Potential for both symptomatic relief and disease modification

Preclinical & research projects

#### Cognition

Cognition encompasses all aspects of intellectual functions and processes such as memory, perception, attention, reasoning, problem solving and decision-making.

Impaired cognition is strongly associated to dementia.

## IRL1117: Next generation treatment of Parkinson

## Aim: long-acting treament for cardinal symptoms in Parkinson disease

- Mono-therapy as well as add on to levo-dopa
- Potential effective treatment without driving complications seen with available treatments (i.e. levodopa)
- Market (16 largest regions): 8.3 million in 2022, expected to increase to 12,9 million in 2040

#### Status

- Nominated in January 2023
- In preclinical development phase
- Phase I ready during 2024







## Finance report Q2 2023

- Highlights and summary
- Analyst coverage

## Financial highlights of Q2 2023

- Maintained focus on cost control
- Investing in the Phase IIb with pirepemat according to plan
- Maintaining investment in preclinical development, advancing IRL757 and IRL942 and IRL1117 towards clinical Phase I
- Cash position SEK 156 million





## Analyst coverage



• Fredrik Thor and Kevin Sule

+46 (0) 545 013 30 info@redeye.se

**ABG** SUNDAL COLLIER

Dr Gonzalo Artiach Castañón

+46 (0)8 566 286 00



- BRILLIANT KNOWLEDGE
- Soo Romanoff and Dr Harry Shrives

+44 (0)20 3077 5700 healthcare@edisongroup.com



## **Development portfolio transforming** treatment of people living with Parkinson's

|                        |  | Discovery         | Preclinical | Phase I     | Phase IIa | Phase IIb | Phase III          | Next major event                     |  |  |  |  |
|------------------------|--|-------------------|-------------|-------------|-----------|-----------|--------------------|--------------------------------------|--|--|--|--|
| Mesdopetam<br>(IRL790) | Parkinson's disease levodopa-<br>induced dyskinesia (PD-LIDs)<br>D3 antagonist |                   |             |             |           |           | Phase III<br>ready | • End-of-Phase 2<br>meeting with FDA |  |  |  |  |
|                        | <b>Parkinson's disease Psychosis</b><br>D3 antagonist                          | Phase I III       |             |             |           |           |                    |                                      |  |  |  |  |
| Pirepemat              | <b>Parkinson's disease impaired<br/>balance and falls</b><br>PFC enhancer      |                   |             |             |           | P         | hase IIb           | <b>H1 2024:</b><br>Top-line data     |  |  |  |  |
| (IRL752)               | <b>Parkinson's disease Dementia</b><br>PFC enhancer                            |                   |             |             |           | Phase IIa |                    | Phase IIb study                      |  |  |  |  |
| IRL757*                | Apathy in neurology  |                   | F           | Preclinical |           |           |                    | <b>YE 2023:</b><br>Phase I ready     |  |  |  |  |
| IRL942*                | Cognitive impairment in neurology  |                   | P           | reclinical  |           |           |                    | H1 2024:<br>Phase I ready            |  |  |  |  |
| IRL1117                | Parkinson's disease<br>treatment   |                   | F           | Preclinical |           |           |                    | <b>2024:</b><br>Phase I ready        |  |  |  |  |
|                        | * Under evaluation under exclusivity l   | by MSRD, an Otsuk | a company.  |             |           |           |                    | 40                                   |  |  |  |  |

**4**U

Portfolio

## Anticipated key development milestones the next 12 months

|   | Q3 2023   | $\rangle$ | Q4 2023  | > | H1 2024  |
|---|---|-----------|--|---|--|
| • | Mid-July: 1st DSMB review and<br>recommendation to continue<br>Phase IIb study with pirepemat<br>Aug 21: Secured ownership of<br>mesdopetam<br>Aug 28: Presentation of Phase<br>IIb study results of<br>mesdopetam at MDS Congress<br>Aug: International<br>acknowledgement of IRLAB<br>competence in use of machine<br>learning in drug<br>discovery/development | • • •     | <ul> <li>2nd DSMB review of the Phase<br/>II study of pirepemat</li> <li>Pirepemat patient recruitment<br/>estimated to be completed by<br/>end of year</li> <li>IRL757 to be Phase I ready</li> <li>Capital Markets Day</li> <li>Participation at investor events<br/>(ABGSC, Pareto, Redeye,<br/>BioStock, SEB)</li> <li>Participation at scientific<br/>congress</li> </ul> |   | <ul> <li>Pirepemat Fas IIb top-line<br/>resultat</li> <li>IRL942 Phase I ready</li> <li>IRL1117 preparation for Phase I</li> </ul> |

Events without confirmed timeframe: - End-of-Phase 2 meeting with the FDA for mesdopetam

### IRLAB – a world-leading portfolio to improve Parkinson's treatments

| Pioneering<br>biology & ISP   | Focused strategy  | Validated business<br>model based on clinical<br>proof-of-concept                                     | Broad & Solid<br>portfolio   | Organization<br>positioned for<br>success                                    |
|---|---|---|--|--|
| Deep profound<br>understanding of<br>Parkinson's. Team<br>from Nobel laurate<br>Prof. Arvid<br>Carlsson's<br>research group | Discover and<br>develop<br>treatments for PD<br>patients<br>throughout their<br>disease journey | From discovery<br>through Phase I<br>and Phase II to<br>Phase III ready<br>projects and<br>dealmaking | Five unique drug<br>candidates each<br>with blockbuster<br>potential<br>generated by our<br>disruptive ISP<br>platform | Experienced<br>international<br>organization.<br>Listed Nasdaq<br>Stockholm. |



Contact:

Gunnar Olsson, CEO, gunnar.olsson@irlab.se

Nicholas Waters, EVP and Head of R&D, nicholas.waters@irlab.se

Viktor Siewertz, CFO, viktor.siewertz@irlab.se

IRLAB is discovering and developing a portfolio of transformative therapies targeting all stages of Parkinson's disease. The company has its origin in Nobel Laureate Prof. Arvid Carlsson's research group and the discovery of a connection between the brain's neurotransmitters and CNS disorders. Mesdopetam (IRL790), in development for the treatment of levodopa-induced dyskinesias, has completed Phase IIb and is in preparation toward Phase III. Pirepemat (IRL752), is currently in Phase IIb, being evaluated for its effect on balance and fall frequency in Parkinson's disease. In addition, the company is also progressing the three preclinical programs IRL942, IRL757, and IRL1117 towards Phase I studies. The pipeline is driven by IRLAB's proprietary systems biology-based Integrative Screening Process (ISP) research platform. Headquartered in Sweden, IRLAB is listed on Nasdaq Stockholm (IRLAB A).

Website: irlab.se | Follow us on LinkedIn >

