

Transforming life for people living with Parkinson's

2022 Q4 and Year-end summary

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Today's agenda



- Opening words
- News in the period



R&D update

- Mesdopetam
- Pirepemat
- Preclinical programs



- Portfolio
- Newsflow & events



Financials

- Financial highlights
- Analyst coverage



Q&A session

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Opening words

- Organizational changes
 - Management
 - Board
- Way forward
 - Working closely with management team
 - Focus on strategic priorities
 - Partnering and business development

Our 2023 strategic priorities

- 1. Fully describe the potential of mesdopetam to be an effective treatment for people in Parkinson's disease.
- 2. Publish and present the comprehensive results of the Phase IIb trial of mesdopetam in Parkinson's disease at scientific congresses and in scientific journals during 2023.
- 3. Pursue the timely completion of the Phase IIb study of pirepemat in PD-Falls.
- 4. Progress IRL942, IRL757 and IRL1117 towards Phase I clinical studies.

Operational highlights in the fourth quarter

- Solid progress in clinical, preclinical and research projects, according to plan
- Phase IIb study of mesdopetam in people with Parkinson's levodopa-induced dyskinesias (PD-LIDs)
 - Fully recruited
 - Database lock year-end 2022
 - Top-line results reported in mid January 2023
- New preclinical data was published providing insight into the mechanisms underlying antipsychotic and antidyskinetic efficacy of drug candidate mesdopetam (IRL790) in PD-Psychosis and PD-LIDs by an independent academic research group led by Prof. Per Petersson at Lund and Umeå University and presented at the premier congress Neuroscience 2022.
- Presentations at **several national and international investor events**: DNB Nordics Healthcare Conference, LSX Inve\$tival Showcase, Redeye Life Science Day and SEB Annual Healthcare Summit. Public recordings are available on the website, irlab.se.



Operational highlights after end of period

- IRLAB **participated at the 6th Neuroscience Innovation Forum** hosted by Sachs Associates in early January, held in connection to the Annual J.P. Morgan Healthcare Conference, in San Francisco, US.
- Drug candidate IRL1117 was nominated from the P003 research project in early January. IRL1117 will be developed as a once-daily oral treatment for the hallmark symptoms of Parkinson's without inducing the troublesome complications caused by today's mainstay anti-Parkinson's levodopa treatments.
- The **top-line results from the Phase IIb study of mesdopetam** in people with Parkinson's disease levodopainduced dyskinesias (PD-LIDs) were announced in mid-January. Mesdopetam demonstrated dosedependent anti-dyskinetic effects in several dyskinetic assessment scales with an adverse event and tolerability profile similar to placebo, even though the study did not statistically meet the primary efficacy endpoint of "good ON"-time. Additional analysis of the full data is currently ongoing.
- In mid-February, the company **announced an update to the portfolio development milestones** following an assessment of the operational priorities for 2023.



Q4 update

Objectives at different stages of clinical development



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Financial highlights in the fourth quarter

- Net sales recorded:
- Total operating expenses:
- The operating result:
- Cash flow from operations:
- Cash and cash equivalents at the end of the period:
- The total number of registered shares:

SEK 12.2m (SEK 12.1m) SEK 45.8m (SEK 35.0m) SEK -33.1m (SEK -23.1m) SEK -37.9m (SEK -28.4m) SEK 252.8m (SEK 401.897m)

51,868,406 (51,748,406)

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



IRLAB – at a glance

		PSEN Innovation for patient care		
Pioneering biology & ISP	Focused strategy	Validated proof- of-concept	Broad & Solid portfolio	Organization positioned for success
Deep profound understanding of Parkinson's based on research by Nobel laurate Prof. Arvid Carlsson	Treating PD patients throughout disease journey, has blockbuster potential as a pharma business	One clinical program already licensed to pharma \$363m + royalties	Five unique drug candidates each with blockbuster potential generated by our disruptive ISP platform	Experienced international organization, Strong Balance sheet, Listed Nasdaq 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)		
Bradykinesia Slowness of moving		Levodopa (in combination with agonists, COMTinhibitors and MAO-B inhibitors)		
Rigidity	Stiffness	Levodopa (in combination with agonists, COMTinhibitors and MAO-B inhibitors)		
Postural instability	$\langle \rangle$ 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.



Parkinson's and IRLAB's solutions

IRLAB to address top priorities for management of Parkinson's

2040

12.9

million

diagnosed

Parkinson's is one of the fastest growing disorders

2015 6.2 million diagnosed

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The burden of society from PD in the US alone translates to \$51,800 per year per patient with Parkinson¹



Pipeline generated with our unique proprietary drug discovery platform – ISP

Integrative Screening Process (ISP)

- Advanced systems biology approach
- Drug design informed by machine learning techniques
- ISP predicts drug candidates with greatest benefit potential and lowest toxicity risk, based on best biological fit.

Proven advantages

- Discovery of truly novel first-in-class compounds
- Strong IPR
- Improvement in probability of drug discovery success and clinical phase transitions, compared with industry standard



ISP predictions: Based on dose response data for each compound 24 neurotransmission related biomarkers, 40 gene expression biomarkers and 308 behavioral descriptors (ca 1400 drugs, other reference compounds & IRLAB compounds from ISP database)

ISP

Living with Parkinson's: IRLAB transforms the treatment algorithm



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

* Currently in development with partner Ipsen who holds an exclusive global 14 license to develop and commercialize mesdopetam





Mesdopetam (IRL790)

- Mesdopetam counteracts levodopa-induced dyskinesias (PD-LIDs) by inhibiting dopamine D3 receptors
- Potential treatment and prevention of psychosis in Parkinson's (PD-P)
- Ipsen licensed the exclusive global rights to develop and commercialize mesdopetam

Currently in development with partner Ipsen who holds an exclusive global license to develop and commercialize mesdopetam (<u>https://www.irlab.se/press-releases/ipsen-and-irlab-enter-exclusive-worldwide-licensing-agreement-aimed-to-improve-the-lives-of-people-livingwith-parkinsons-disease//</u>)

Mesdopetam's clinical development plan

Study	Study Population	Treatment duration	Design	# subjects	Primary objectives	Status	Result
Ph I: SAD+ MAD	Healthy male volunteers	SAD+MAD 10 days	DB placebo controlled cross- over	16 (SAD) 24 (MAD)	PK, safety, tolerability	Finalized	Tolerable, good safety, linear PK, up to 120 mg/day in the SAD part and up to 80mg/day in the MAD part
Ph Ib (patients)	PD-LIDs (dyskinesia)	4 weeks	DB placebo controlled	15 (3:1 allocation)	Tolerability, PK, safety, UDysRS, PKG (actigraph), UPDRS	Finalized	Mesdopetam can be safely administered to patients with advanced PD. Assessments for motor function showed a numeric reduction in dyskinesia across assessments
Ph IIa	PD-LIDs (dyskinesia)	4 weeks	DB placebo controlled	74	UDysRS, CGI, MDS- UPDRS, Hauser diary	Finalized	Mesdopetam is tolerable and displays good safety. AEs were predominantly central nervous system related, mild, and predominantly reported during the first 2 weeks of treatment Aggregated doses of mesdopetam 2.5, 5, 7.5 mg (b.i.d) improved "good ON"-time by ~2.8 hours (p=0.002)
Ph IIb	PD-LIDs (dyskinesia)	12 weeks	DB placebo controlled	154	Primary EP: Change in average daily hours of ON-time without troublesome dyskinesia	Fully recruited. Top-line data YE	Dose finding successful. Preferred dose 7.5 mg b.i.d. Did not meet significance on primary endpoint. Objective UDysRS showed consistent and statistically significant effects. Improvement in UPDRS scale measuring disability associated with dyskinesia. Dose dependent reduction in OFF. No impairment of normal motor function. AE profile like placebo.
Phase III*	- PD-LIDs (dyskinesia) - PD-P	Post Phase III	o data, Ipsen is resj	ponsible for the fu	rther decisions regarding d	evelopment and	d commercialization



Mesdopetam

Growing body of clinical evidence supporting potential as treatment of dyskinesia in PD



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



Pirepemat

Why preventing falls in Parkinson's?

Reducing falls is the greatest medical need and one of the worst aspects of Parkinson's.

- Prospective studies report that 70% of people with Parkinson's have at least one fall in a year and about 45% fall recurrently.
- Median survival in patients that have recurrent falls is 6 years.
- Reasons why people with Parkinson's fall^{1,2}:

Cognitive decline → Impaired balance → Falls → Injuries & costs

 Consequences of falls include fractures and injury, fear of future falls, hospital admission, and increased caregiver burden, with falls cited as one of the worst aspects of the disease.



Fall injuries are the dominant cause of hospitalization for people with Parkinson's

Pirepemat

Pirepemat can improve balance and reduce falls in Parkinson's

- A large unmet need
- 45% of all people with Parkinson's fall recurrently
- Impaired balance and a fear of falling significantly impair the daily lives of many with Parkinson's
- **Pirepemat is designed to improve balance and reduce falls** by strengthening nerve cell signalling in the cortex via action at 5HT7 and alpha-2 receptors
- The **cost of treatment for a fall** injury is estimated to about **30,000 USD** in people over age 65



IRLAB addresses a new, untapped market

Impaired balance leading to falls in Parkinson's have high prevalence and represent a great unmet medical need. There are currently no approved drugs.

Pirepemat

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

Mechanism of Action	Combines antagonism at 5HT7 and alpha-2 receptors leading to highly specific activation of frontal cortex NA and DA	Volume 374 Number 3 September 2020 ISSN 1521-0103
Tolerability	 Well tolerated in clinical studies Dose range defined 	PHARMACOLOGY And Experimental Therapeutics
Efficacy	• Pirepemat shows promising improvements of balance and has potential to reduce falls in Parkinson's by 50%	Chemical structure and <i>in vitro</i> profile of IRL752 S-HT7 25 µM 20 µM 15 µM 30 µ 30
Regulatory	 Ongoing Phase IIb program developed with regulatory agencies, scientific advisors and regulatory experts EU regulatory agencies: Study and ethical approvals granted; study ongoing. FDA advice to conduct additional DMPK and in vitro mechanism studies, prior to US IND. These studies are expected to be finalized Q2 2023 	SIM MOR MOR MAT S-HTZA S-HTZC S-HTZC
Potential	 About 50% of patients with Parkinson's fall (Hoehn&Yahr stage ≥ 3) Health economic data show cost of falls are very high 	A Publication of the American Society for Pharmacology and Experimental Therapeutics
Validation	 WHO-INN proposes new INN, pirepemat (generic name) representing a new CNS compound class = first-in-class Studies published in highly ranked scientific journals 	About the cover: Pirepemat featured on the cover of the Sep 2020 issue of JPET
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Pirepemat's clinical development plan

Study	Study Population	Treatment duration	Design	# subjects	Primary objectives	Status	Result
Ph I: SAD+ MAD	Healthy male volunteers	SAD+MAD 10 days	DB placebo controlled alternate panel design	16 (SAD) 24 (MAD)	PK, safety, tolerability	Finalized	Single and multiple doses of pirepemat were generally well tolerated. The safety, tolerability, and PK profiles in this study support 3-times-daily dosing and further clinical development.
Ph I new PK tablet formulation	Elderly male and female healthy volunteers Average 72 years	MAD 14 days	Open label	9	Pharmacokinetics Tablet formulation	Finalized	The half-life of pirepemat may be longer, and plasma exposures somewhat higher, in elderly subjects as compared to younger subjects. No SAEs occurred in the study and there were no clinically significant abnormal findings in any of the clinical safety parameters. Elevated plasma liver enzymes levels following discontinuation of study treatment were seen in some individuals.
Ph Ila	Patients with Parkinson's disease and dementia	4 weeks	DB placebo controlled	32 (3:1 active vs. placebo)	Falls frequency as compared to placebo Cognitive function MDS-UPDRS, NPI, CGI Balance tests	Finalized	Pirepemat appears to be safe and well tolerated during 4-week treatment in study population. Adverse events were predominantly central nervous system related, mild, and predominantly reported during the first 2 weeks of treatment. Elevated liver enzymes observed in three pts following discontinuation. The interpretation is that this is part of a rebound effect following an abrupt termination of treatment with pirepemat.
Ph IIb	Parkinson's patients at H&Y stage >2,5. with MoCA<26 At least 2 falls 1 mo prior to randomization	12 weeks	DB placebo controlled	165	Reduction in falls frequency MoCA, UPDRS II+III, CGI-S	Ongoing	Recruiting in France, Germany, Poland Spain & Sweden.



Clinical Phase IIb: Improve balance and reduction of falls

"A Phase IIb to evaluate the effects of pirepemat on falls frequency as compared to placebo."

Study IRL752C003

Primary objective

• To evaluate the effects of pirepemat on **falls frequency** as compared to placebo.

Secondary & other objectives

- To evaluate the effects of pirepemat on cognitive functions assessed with Montreal Cognitive Assessment (MoCA), as compared to placebo.
- To evaluate the effects of pirepemat on Parkinson's disease symptoms assessed with Unified Parkinson's Disease Rating Scale (MDS-UPDRS) as compared to placebo.
- To evaluate the effects of pirepemat on **postural dysfunction**, tandem walking and single leg stance test compared to placebo.
- To evaluate the effects of pirepemat on **global function** assessed with Clinicians Global Impression of Severity (CGIS), as compared to placebo.
- To examine the relationship between dose and plasma concentration of pirepemat and pharmacodynamic effects.

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

Primary endpoint

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- Evaluate the effects of pirepemat on falls frequency as compared to placebo
- Efficacy assessed by Falls diaries, motor function, Cognitive and balance assessments as well as a CGIS

Data expected H1 2024



Protocol considerations: Dose de-escalation and specific exclusion criteria are applied in the protocol to limit the impact of rebound effect on liver enzymes after abrupt discontinuation of study medication



Preclinical & Research projects

- IRL757 Clinical candidate Treat apathy
- IRL942 Clinical candidate
- IRL1117 Clinical candidate
- Improve cognitive function and
- Improve cognitive function and brain health
 - Once-daily oral treatment of Parkinson's without troublesome complications



Ongoing preclinical development programs on track

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

Scientific rationale of IRL942 & IRL757

Problem

Disruption of frontal neurotransmission is implicated in the pathogenesis of cognitive decline and neuro-psychiatric symptoms in PD and other neurological disorders

No current treatments directly address these specific cortical deficiencies

IRLAB's solution

IRL942 and IRL757 show a unique ability to activate frontal neurotransmission, synaptic gene expression, and associated circuits, improving cognitive function across modalities

Potential for both symptomatic relief **and** disease modification

Potential clinical indications:

- Parkinson's disease: dementia, apathy, depression, attention/vigilance
- Besides PD dementia, data support potential in additional indications with unmet needs:
- Other dementias

Cortical synaptic dysfunction a hallmark in multiple dementia types

- Lewy body dementia, Alzheimer's disease, Vascular dementia, Frontotemporal dementia, Age related cognitive decline/MCI
- Apathy & Depression
 - Apathy: Cortex crucial in control of motivation, mood, cognition, and social behavior
 - Depression: Disruption of PFC signaling implicated in the pathogenesis
- ADHD
 - Cortical weakness in NA/DA transmission no cortically targeted treatments available today
- Schizophrenia
 - Difficult-to-treat pathology converges on cortical dysfunction negative and cognitive symptoms

IRL1117 – First orally active, full efficacy, long-acting Parkinson's treatment

- Current treatment of Parkinson's is based on levodopa
- Limitations of levodopa
 - Short duration of action warrants multiple daily administrations leading to complications
 - Excessive stimulation and involuntary movements
 - 'On-off'-fluctuations (periods of absent effect)
- Levodopa supplemented by add-on medications:
 - Dopamine D₂ agonists
 - Long duration of action but inferior efficacy
 - Enzyme inhibitors
 - Provides minor extension of levodopa duration of action
 - Apomorphine
 - D_1/D_2 agonist high efficacy but poor PK and not orally bioavailable
 - Available as acute rescue during 'off'-periods or chronically implanted pump





Finance report Q4 2022

- Highlights and summary
- Analyst coverage

Financial highlights of Q4 2022

- Sustained focus on cost control
- Investing in pirepemat clinical Phase IIb according to plan
- Maintaining investment in preclinical development, advancing IRL757 and IRL942 and IRL1117 towards clinical Phase I
- Stable cost base (Q2 2022 through Q4 2022) at about SEK 40 million per quarter
- Cash position SEK 253 million



Partnering cost: Cost for entering licensing agreements and costs which are covered by a corresponding revenue from partners.

Analyst coverage



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Portfolio transforming treatment of people living with Parkinson's

		Discovery	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Next major event
Mesdopetam (IRL790)*	Parkinson's disease levodopa- induced dyskinesia (PD-LIDs) D3 antagonist					P	hase IIb	Ipsen disposition r.e. further
	Parkinson's disease Psychosis D3 antagonist		Phase I					development
Pirepemat (IRL752)	Parkinson's disease impaired balance and falls PFC enhancer					P	hase IIb	~ H1 2024: Top-line data
	Parkinson's disease Dementia PFC enhancer			Phase IIa				Phase IIb study
IRL942	Cognitive impairment in neurology			Preclinical				2023: Phase I ready
IRL757	Apathy in neurology			Preclinical				2024: Phase I ready
IRL1117	Parkinson's disease treatment			Preclinical				2023: Preclinical development
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Anticipated newsflow and events the next 18 months

	Q1 '23	Q2 '23	H2 ′23	H1 '24
Milestones	 IRL1117 CD nomination Mesdopetam Phase IIb top- line results 	 Mesdopetam additional Phase IIb study results 	 IRL757 Phase I ready Pirepemat Phase IIb completes recruitment IRL942 Phase I study preparation 	 Pirepemat Phase IIb top-line results IRL942 Phase I ready IRL1117 Phase I study preparation
Events	 8 March: ABGSC Investor Day, SthIm 28 March-1 April: AD/PD 2023 congress, Gothenburg 	 22-28 April: AAN congress, Boston Participation at investor events 	 Capital Markets Day Participation at medical congresses Participation at investor events 	 Participation at medical congresses and investor events
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IRLAB discovers and develops novel drugs for the treatment of Parkinson's disease and other disorders of the brain. The company's most advanced drug candidates, mesdopetam (IRL790) and pirepemat (IRL752), both of which are currently subject to Phase IIb studies, were designed to treat some of the most difficult symptoms associated with Parkinson's disease. In 2021, IRLAB entered into an exclusive global license agreement with Ipsen regarding the development and commercialization of mesdopetam. Through its proprietary research platform, ISP (Integrative Screening Process), IRLAB has discovered and developed all its projects and keeps discovering innovative drug candidates for the treatment of disorders of the central nervous system (CNS). In addition to IRLAB's strong clinical development portfolio, IRLAB runs several preclinical programs, with IRL942, IRL757 and IRL1117 in development for Phase I studies.

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