Press Release

Göteborg August 21, 2023

IRLAB provides update on mesdopetam's Phase IIb study data and the plans toward Phase III

Gothenburg, Sweden, August 21, 2023 – IRLAB Therapeutics AB (Nasdaq Stockholm: IRLAB A), a company discovering and developing novel treatments for Parkinson's disease, today announced further information on the results from mesdopetam's clinical Phase IIb study in Parkinson's disease levodopa-induced dyskinesias (PD-LIDs) and Phase III preparatory Phase I studies performed by Ipsen. The results indicate that mesdopetam has dose-dependent anti-dyskinetic and anti-parkinsonian effects combined with a tolerability and safety profile not different from placebo, giving mesdopetam a unique position in the competitive landscape. The comprehensive data package developed by IRLAB and Ipsen provides a solid foundation for continuing the development of mesdopetam to Phase III. IRLAB now proceeds with preparations for Phase III, requesting an end-of-Phase 2 meeting with the US FDA to define the Phase III study program. A webcast in conjunction with the announcement will be held on August 22, 2023, at 10:00 CEST, access details below.

In-depth analyses of the Phase IIb study data have now been completed confirming the great potential of mesdopetam in people living with PD-LIDs. The objectives of the study were to investigate the efficacy and safety of three doses of mesdopetam (2.5, 5, and 7.5 mg twice daily (b.i.d.)), as compared to placebo, in people living with PD-LIDs to guide dose selection for Phase III. Top-line results from the Phase IIb study of mesdopetam in PD-LIDs were communicated in January 2023.

In the in-depth evaluation of the Phase IIb study data the effects in subjects based both on their randomized dose (FAS population) and based on the actual dose received in subjects compliant with the protocol (PS population), were analyzed. Since dose adjustment was allowed at one time during this study, analyses based on the actual dose received are important to get a full understanding of the dose dependency and the treatment effects. These analyses provide the basis for dose selection for Phase III.

"We are pleased to see clear and clinically meaningful anti-dyskinetic effects of mesdopetam in the analyses of the Phase IIb study data. Consistent dose-response patterns were observed across the key efficacy endpoints assessing dyskinesia: "good ON"-time, UDysRS, UDysRS subscales. This, in combination with unchanged MDS-UPDRS part 2 scores demonstrates that mesdopetam

shows anti-dyskinetic efficacy without affecting normal motor function, or negatively impacting the anti-parkinsonian treatment effect of levodopa. The reduced OFF-time even indicates that mesdopetam has anti-parkinsonian effects," said Nicholas Waters, EVP and Head of R&D, IRLAB. "The dose-dependent effects make it possible to select dose for Phase III."

In the FAS, mesdopetam's treatment effect on Hauser diary "good ON" (ON-time without troublesome dyskinesia) did not reach statistical significance, whereas in the PS, among subjects taking the 7.5 mg b.i.d. dose of mesdopetam, a significant and clinically meaningful increase in "good ON"-time of 1.75 hours vs placebo ("good ON" scaled to 16 hours awake time, p=0.050) was observed.

In the FAS, mesdopetam demonstrated significant anti-dyskinetic effects, as measured by UDysRS, sum of parts 1, 3 and 4, with a reduction of 6.2 points vs. placebo (p=0.026) at 7.5 mg b.i.d. In the PS, the effect on UDysRS was dose-dependent and a reduction of 9.2 points vs. placebo (p=0.011) was observed at 7.5 mg b.i.d. In the UDysRS disability score parts 1b+4, assessing the degree of disability caused by dyskinesia, there was a reduction of 3.5 points vs. placebo (p=0.062) in the FAS and, in the PS a reduction of 5.5 points vs placebo (p=0.019) was observed at 7.5 mg b.i.d.

This means that both patients and physicians report reduced disability related to dyskinesia during mesdopetam treatment. Further, the daily time spent in OFF showed a clear dose-dependent pattern and a decrease compared to placebo in both FAS and PS, reaching 1.27 hours (p=0.051) at the 7.5 mg b.i.d. dose in the PS, indicating a direct anti-parkinsonian effect of mesdopetam in subjects treated with levodopa. Mesdopetam was well tolerated with an adverse event and safety profile on par with placebo.

"I think the mesdopetam data package is one of the most compelling available in the symptomatic treatment of Parkinson's. Mesdopetam has the rare ability to both improve dyskinesias and improve parkinsonism and, at the same time, appears to be well tolerated. I expect it will have both clinical utility and commercial success," said Karl Kieburtz, MD, MPH, Professor in Neurology, Former chairman of the Peripheral and Central Nervous System US FDA Advisory Committee; chairman of the Scientific Evaluation Committee for the Cooperative Studies Program, Veterans Administration, and the National Institute of Neurologic Disorders and Stroke.

The Phase I clinical studies performed by Ipsen to prepare for Phase III were successfully completed and showed favorable results. One study evaluated pharmacokinetics (PK) in different populations showing that mesdopetam has similar PK in Asian and Non-Asian populations. A second study evaluated the potential for PK drug-drug interactions, via key drug metabolizing enzymes, showing a low risk of drug-drug interaction, suggesting that neither additional clinical drug-drug interaction studies nor restrictions on future patient enrolment would be required in future clinical studies. A third study investigated elimination routes of mesdopetam showing no risk of accumulation of mesdopetam in the body. Safety data from all three studies did not reveal

any new safety signals and thus, was consistent with the current knowledge of the safety profile for mesdopetam.

"The data from the three Phase I studies performed by Ipsen are encouraging as they suggest that treatment with mesdopetam will be predictable and with little variability. This will most likely result in a simple uniform dosing of the drug, which minimizes the risk of dosing errors and is an advantage for mesdopetam over current alternatives in the management of dyskinesia in Parkinson's," commented Joakim Tedroff, CMO, IRLAB.

"I am excited by the potential of mesdopetam both commercially and how it truly can benefit people living with Parkinson's. The aging global population driving the increased prevalence of Parkinson's and people developing levodopa-induced dyskinesia suggest that mesdopetam could play an important role in this large and growing unmet clinical need. I will focus on leading the continued work toward Phase III together with our regulatory, clinical, and financial advisors. We anticipate that this strengthening of our portfolio with the Phase III ready mesdopetam project will improve our partnering and financing opportunities to advance our world-leading portfolio of treatments in Parkinson's disease," said Gunnar Olsson, CEO, IRLAB.

In conclusion, available data indicate that mesdopetam has dose-dependent anti-dyskinetic and anti-parkinsonian effects combined with a tolerability and safety profile not different from placebo, giving mesdopetam a unique position in the competitive landscape. The comprehensive data package developed by IRLAB and Ipsen provides a solid foundation for continuing the development of mesdopetam to Phase III. IRLAB now proceeds with preparations for Phase III, requesting an end-of-Phase 2 meeting with the US FDA to define the Phase III study program.

Comprehensive results of the Phase IIb study of mesdopetam in PD-LIDs will be presented at MDS Congress in Copenhagen held on August 27-31, 2023. As IRLAB secured full ownership of the mesdopetam project, all further communications concerning mesdopetam are now the responsibility of IRLAB.

For more information

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Webcast for investors, analysts, and media

The company will hold a live webcast in conjunction with the announcement on August 22, 2023 at 10:00 CEST.

Access webcast via link: https://channel.royalcast.com/landingpage/hegnarmedia/20230822_4/

About the Full Analysis Set (FAS)

The Full Analysis Set (FAS) consisted of all randomized and treated patients who received one or more doses and who provided post-baseline data independent of the actual dose taken during the study, also commonly referred to as the ITT analysis.

About the protocol-compliant adjusted dose set (PS)

The protocol-compliant adjusted dose set (PS) consisted of patients who were compliant to the study protocol including documented compliance to the dosing regimen in the study, with adjustment to the actual dose received.

About Hauser diary (patient-completed 24-hour diaries)

Clinical diaries are a standardized method for patients to assess their health status. Patients log their motor status every 30 minutes for 24 hours. Patients record whether their motor status is:

- "OFF" denotes stiffness, marked decrease of mobility or immobility
- "ON" denotes good or practically normal mobility
- "ON with troublesome dyskinesias" is when the patient is troubled by involuntary twisting and turning movements.
- Additionally, sleep time is recorded

About Unified Parkinson's Disease Rating Scale (MDS-UPDRS)

The Unified Parkinson's Disease Rating Scale (MDS-UPDRS) is a standardized and validated estimation scale developed for assessment of symptoms in Parkinson's disease. The instrument has been tested for good reliability and validity and consists of the following four parts:

- Part I – Non-Motor Aspects of Experiences of Daily Living
- Part II – Motor Aspects of Experiences of Daily Living
- Part III – Motor Examination
- Part IV – Motor complications of therapy

Each section has questions that rate the symptoms from 0 to 4 where higher values indicate more severe symptoms.

About Unified Dyskinesia Rating Scale (UDysRS)

The Unified Dyskinesia Ratings Scale (UDysRS) evaluates the involuntary movements that can be associated with long-term treatment with dopaminergic medication. The UDysRS has four parts:

- Part 1 – Historical Disability (patient perceptions) of ON-Dyskinesia impact
- Part 2 – Historical Disability (patient perceptions) of OFF-Dystonia impact
- Part 3 – Objective Impairment (dyskinesia severity, anatomical distribution over seven body regions, and type (choreic or dystonic) based on four activities observed or video-recorded
- Part 4 – Objective disability based on Part III activities

The modified UDysRS was used in the Phase IIb trial, which constitutes Part 1, Part 3 and Part 4.

About Phase IIb study with mesdopetam

The Phase IIb study with mesdopetam in people with Parkinson's disease affected by levodopa-induced dyskinesias (LIDs) was a randomized, double-blind, placebo-controlled study with the purpose of evaluating anti-dyskinetic effect and safety/tolerability of three different doses of mesdopetam and to define the right dose of the drug for Phase III studies. Subjects on stable regimen of anti-parkinson medication, experiencing troublesome dyskinesia, were randomized to placebo, mesdopetam 2.5, 5, or 7.5 mg b.i.d. for 12 weeks. According to the study protocol patients were allowed to adjust their dose one time during the study. The primary endpoint was daily ON-time without troublesome dyskinesia ("good ON") measured by Hauser-diaries. Secondary endpoints included UDysRS (parts 1+3+4), UDysRS disability score (1b+4), UDysRS objective score (3+4), time in different motor-states (bad ON, OFF), MDS-UPDRS, CGI, MMSE, along with pharmacokinetics, safety and tolerability. Data presented here was analyzed based on least squares mean (LS mean) differences vs. placebo using a mixed models for repeated measures (MMRM) for the Full Analysis Set (FAS) based on randomized dose, and in the protocol compliant subjects with adjustment to actual dose received (PS). To adjust for variability in sleep time, Hauser diary data were also scaled to 16 hours of awake time in the PS (post-hoc).

The study randomized 156 patients distributed across four groups, three dose levels of mesdopetam and a placebo group with approximately 40 patients in each group with a treatment period of three months. The study was conducted at 46 study sites in Europe, Israel and in the US. More information can be found on clinicaltrials.gov: NCT04435431, and EudraCT number: 2020-002010-41.

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About mesdopetam

The investigational drug mesdopetam (IRL790) is a dopamine D3 receptor antagonist in development as a treatment of Parkinson's disease levodopa-induced dyskinesias (PD-LIDs). The primary objective of mesdopetam is to improve the quality of life of individuals with Parkinson's disease by reducing PD-LIDs, a debilitating condition characterized by involuntary movements that frequently develop in patients who receive prolonged/chronic levodopa treatment. The results of the completed clinical studies in the Phase I and Phase II programs demonstrate a consistent anti-dyskinetic effect of mesdopetam, good safety, and it is assessed as offering significantly better tolerability compared to existing treatments.
Preclinical studies show that mesdopetam is a potent and efficacious anti-dyskinetic drug, and that mesdopetam also has the potential to prevent the development of dyskinesia as well as treating Parkinson's disease Psychosis (PD-P).

About IRLAB

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). For more information, please visit www.irlab.se.

Attachments

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