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News Release

Not intended for UK Media

AskBio presents 18-month Phase Ib trial results of AB-1005 gene therapy for patients with Parkinson's disease

- AB-1005 (also known as AAV2-GDNF), an investigational gene therapy for the treatment of Parkinson's disease, was well tolerated with no attributed serious adverse events in all 11 patients at 18 months, meeting the primary objective
- Based on the safety and efficacy results presented, a Phase II trial (REGENERATE PD) has been developed and is expected to begin enrolling in the U.S., EU, and UK later this year

Berlin, Germany, and Research Triangle Park, NC, USA, April 16, 2024 – Bayer AG and Asklepios BioPharmaceutical, Inc. (AskBio), a gene therapy company wholly owned and independently operated as a subsidiary of Bayer AG, on Sunday April 14 presented results from the 18-month Phase Ib clinical trial for AB-1005, an investigational gene therapy for treating patients with Parkinson's disease (PD).[1,2] The data were presented at the American Academy of Neurology 2024 Annual Meeting in Denver, Colorado, USA.

The study met its primary objective, which was to evaluate the safety of a one-time bilateral delivery of AB-1005 directly to the putamen. Eleven patients were enrolled into two cohorts, Mild stage PD (6 patients) and Moderate stage PD (5 patients), based on timing from PD clinical diagnosis and the severity of PD symptoms at trial screening.[1]

As of November 3, 2023, 57 nonserious adverse events (AEs) and 6 serious adverse events (SAEs) were reported. Most AEs were transient and were expected perioperative events (<1 month from treatment). These included headache, tremor, dyskinesia, arthralgia, musculoskeletal chest pain, fatigue, COVID-19, and magnetic resonance imaging (MRI) abnormalities. The 6 SAEs reported in 3 patients (n = 1 in the Mild Cohort and n = 2 in the Moderate Cohort) were all assessed as unrelated to the treatment by the Investigator and the Sponsor.

Bilateral infusions of AB-1005 within the putamen (up to 1.8 mL) were well tolerated, with no SAEs associated with the investigational gene therapy or contrast agent. Neurosurgical delivery of AB-1005 resulted in putamen coverage of 63% ± 2%, exceeding the goal of greater than 50% coverage with AB-1005. Scheduled 6-month postoperative MRIs revealed findings of asymptomatic unilateral T1 hypointensity adjacent to 3 of the putaminal infusion trajectories. Clinical follow-up for up to 5 years post administration is ongoing.[2]

“These early findings are encouraging and show AB-1005 to be well tolerated in this study in patients with mild to moderate Parkinson’s disease,” said Krystof Bankiewicz, MD, PhD, Scientific Chair, Parkinson’s and MSA, AskBio. “Further, they highlight areas of potential future exploration in our upcoming Phase II REGENERATE PD trial, which will look more closely at the potential efficacy of AB-1005 in the treatment of Parkinson’s disease.”

Patients also completed 18-month neurological assessments and self-reported questionnaires at regular intervals to evaluate the severity of motor and non-motor symptoms associated with PD.[1]

Mild Cohort

The Movement Disorder Society-Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) is an internationally recognized tool used to assess the severity of PD symptoms, including motor symptoms. The Mild Cohort (n = 6) demonstrated relative stability from baseline to 18 months for both MDS-UPDRS Part II patient-reported Activities of Daily Living scores and Part III clinician-rated Motor Examination scores in “ON” and “OFF” medication states.

Patient-reported PD Motor Diaries provide a tool for assessing patient motor state over an extended 3-day period and then normalized to a 16-hour waking day. The Mild Cohort (n = 5) showed a -1.3 hour reduction in “Good ON” time, a 0.2 hour increase in “ON” time with troublesome dyskinesia, and a 1.1 hour increase in “OFF” time. One patient in the Mild Cohort declined to complete the diary after dosing, while troublesome dyskinesia and increased “OFF” state time in this cohort were driven by another subject with a genetic defect of unknown pathological significance. These factors are believed to have contributed to worsening of "Good ON” state time and “OFF” state time over 18 months for the Mild Cohort.

Levodopa Equivalent Daily Dose (LEDD) is a summary measure of all anti-parkinsonian medications taken over a 24-hour period. The Mild Cohort had a lower LEDD at baseline than the Moderate Cohort and demonstrated further stability of LEDD over 18 months.

Moderate Cohort

MDS-UPDRS scores for the Moderate Cohort (n = 5) demonstrated a Part II Activities of Daily Living mean (standard error) improvement of -3.8 (3.5) points from baseline, and Part III Motor Examination improvements of –20.4 (4.5) points “OFF” medication, and –10.6 (3.6) points “ON” medication compared to baseline. Most PD patients can sense a 3-point reduction of MDS-UPDRS Part III, and the 20.4-point improvement seen in the “OFF” state in the Moderate Cohort is considered to represent a large clinical effect.

Motor Diaries for the Moderate Cohort reported a 2.2-hour improvement in “Good ON” state time, which was clinically meaningful; a 0.5-hour reduction in “ON” state with troublesome dyskinesia; and a 1.7-hour reduction in “OFF” state time. This equates to a 23.6% ± 11.8% increase in “Good ON” state time and a 33.1% ± 17.4% decrease in “OFF” state time in the Moderate Cohort at 18 months.

The Moderate Cohort demonstrated a progressive reduction of dopaminergic medications post-treatment, with a mean 258 ± 162 mg LEDD reduction from baseline. Notably, the motor improvements demonstrated were in the setting of a reduced levodopa requirement.

These outcomes demonstrate that most patients in the Mild Cohort achieved overall clinical stability with little change in MDS-UPDRS and PD Motor Diary outcomes and that participants in the Moderate Cohort achieved clinical motor improvement at 18 months.

AskBio is planning to publish 18-month study results later this year. Based on the top-line 18-month safety and clinical effects results presented, a Phase II trial (REGENERATE PD) has been developed and is expected to begin enrolling patients later this year in the U.S., EU, and UK.

“We are excited to see AskBio’s investigational gene therapy for Parkinson’s disease reach significant milestones in clinical development and look forward to moving into

Phase II later this year," said Christian Rommel, PhD, Head of Research and Development at Bayer's Pharmaceuticals Division. "While much remains to be done, we recognize with increasing confidence the potential of AB-1005 to provide a transformative impact for patients in the future."

About AB-1005

AB-1005 is an investigational gene therapy based on adeno-associated viral vector serotype 2 (AAV2) containing the human glial cell line-derived neurotrophic factor (GDNF) transgene, which allows for stable and continuous expression of GDNF in localized regions of the brain after direct neurosurgical injection with magnetic resonance imaging (MRI)-monitored convection enhanced delivery.[3,4] GDNF is a homodimer that is a distantly related member of the transforming growth factor-β superfamily. In midbrain neuronal cell cultures, recombinant human GDNF promoted the survival and morphological differentiation of dopaminergic neurons and increased their high-affinity dopamine uptake. GDNF has long been evaluated as a potential treatment for diseases, such as Parkinson's, marked by progressive degeneration of midbrain dopaminergic neurons.[5]

About the AB-1005 Phase Ib trial

In this Phase Ib, multi-center, multi-site, parallel assignment, non-randomized trial, 11 patients were administered AB-1005 to the putamen via one-time bilateral convection-enhanced delivery. Patients were enrolled into two cohorts, Mild (6 patients) and Moderate (5 patients), based upon the duration and stage of their PD. The objective of this investigation was to evaluate the safety and potential clinical effect of AB-1005 delivered to the putamen in patients with either a recent or a long-standing diagnosis of PD. The outcomes assessed at 18 months were incidence of Treatment-Emergent Adverse Events (TEAEs) as reported by the patients or assessed clinically by physical and neurological examinations, motor symptoms as reported via the Movement Disorder Society's Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and PD Motor Diary self-assessments, and non-motor symptoms of PD and brain dopaminergic network integrity as measured by DaTSCAN.[1] These assessments will continue for up to five years. For more information, visit clinicaltrials.gov (NCT#04167540), visit askbio.com, or send an email to AskFirst@askbio.com.

About Parkinson's disease

Parkinson's disease is a progressive neurodegenerative disorder caused by the death of nerve cells in the brain, leading to decreased dopamine levels.[6] At diagnosis, it is estimated that patients have already lost 50-80% of their dopaminergic neurons.[7] The loss of these neurons leads to a progressive loss of motor function and symptoms such as tremors, muscle rigidity, and slowness of movement.[8] Even with medication, the symptoms of Parkinson's disease can fluctuate during the course of the day. According to the Parkinson's Foundation, more than 10 million people worldwide suffer from Parkinson's disease[9], with approximately one million living in the United States.[9] There is no cure, and the effectiveness of current treatments frequently decreases over time.[10]

About AskBio

Asklepios BioPharmaceutical, Inc. (AskBio), a wholly owned and independently operated subsidiary of Bayer AG, is a fully integrated gene therapy company dedicated to developing life-saving medicines and changing lives. The company maintains a portfolio of clinical programs across a range of neuromuscular, central nervous system, cardiovascular and metabolic disease indications with a clinical-stage pipeline that includes therapeutics for congestive heart failure, Huntington's disease, limb-girdle muscular dystrophy, multiple system atrophy, Parkinson's disease, and Pompe disease. AskBio's gene therapy platform includes Pro10™, an industry-leading proprietary cell line manufacturing process, and an extensive capsid and promoter library. With global headquarters in Research Triangle Park, North Carolina, and European headquarters in Edinburgh, Scotland, the company has generated hundreds of proprietary capsids and promoters, several of which have entered pre-clinical and clinical testing. An early innovator in the gene therapy field, with over 900 employees in five countries, the company holds more than 800 patents and patent applications in areas such as AAV production and chimeric capsids. Learn more at www.askbio.com or follow us on LinkedIn.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. In line with its mission, "Health for all, Hunger for none," the company's products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its

earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2023, the Group employed around 100,000 people and had sales of 47.6 billion euros. R&D expenses before special items amounted to 5.8 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements
This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

AskBio Forward-Looking Statements
This press release contains "forward-looking statements." Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "will," "intends," "potential," "possible" and similar expressions are intended to identify forward-looking statements. These forward-looking statements include without limitation statements regarding AskBio's clinical trials. These forward-looking statements involve risks and

uncertainties, many of which are beyond AskBio's control. Known risks include, among others: AskBio may not be able to execute on its business plans and goals, including meeting its expected or planned clinical and regulatory milestones and timelines, its reliance on third-parties, clinical development plans, manufacturing processes and plans, and bringing its product candidates to market, due to a variety of reasons, including possible limitations of company financial and other resources, manufacturing limitations that may not be anticipated or resolved in a timely manner, potential disagreements or other issues with our third-party collaborators and partners, and regulatory, court or agency feedback or decisions, such as feedback and decisions from the United States Food and Drug Administration or the United States Patent and Trademark Office. Any of the foregoing risks could materially and adversely affect AskBio's business and results of operations. You should not place undue reliance on the forward-looking statements contained in this press release. AskBio does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

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