AskBio™

The AAvenger™

ADENO-ASSOCIATED VIRUS (AAV) GENE THERAPY NEWS

WINTER 2022 | VOL.6

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Founder of BrainVectis
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BRAINVECTIS, A SUBSIDIARY OF ASKBIO, RECEIVES CLEARANCE TO CONDUCT PHASE I/II CLINICAL TRIAL IN FRANCE FOR ITS NOVEL GENE THERAPY FOR EARLY-STAGE HUNTINGTON'S DISEASE

National Agency for Safety of Medicines and Health Products (ANSM) and French Ethics Committee approve protocol for trial expected to begin in Q4 2022

AskBio, a wholly owned and independently operated subsidiary of Bayer AG, has received clearance to conduct a Phase I/II trial for its novel Huntington's Disease (HD) gene therapy, BV-101, in France through its subsidiary BrainVectis. This authorization, provided by the National Agency for Safety of Medicines and Health Products (ANSM), the country's governing drug authority, along with the approval of the trial protocol by the Ethics Committee in charge, enables the company to begin recruiting participants. BV-101 is a novel, exclusively designed adeno-associated virus (AAV) gene therapy vector that simultaneously addresses the metabolic dysfunction of diseased neurons as well as contributes to the clearance of the mutant huntingtin protein. BV-101 is administered through MRI-guided neurosurgical techniques directed to target tissues in the basal structures of the brain. In preclinical studies in mice, BV-101 demonstrated the ability to repair the essential cholesterol pathway, provide neuroprotection, and restore physical performance by delivering CYP46A1, a crucial enzyme in the brain which is reduced in people with Huntington's Disease. BV-101 was granted orphan drug designation in the European Union in 2019 by the European Medicines Agency.

"Unlike other attempts to treat Huntington's Disease, BV-101 aims to restore cholesterol metabolism, reduce mutant huntingtin and to improve neuronal function. Importantly, BV-101 does not affect the levels of normal huntingtin protein in cells," said Nathalie Cartier-Lacave, MD, founder of BrainVectis and now Vice President, Sector Lead Neurobiology, at AskBio. "If this proves successful, we have the potential to change the course of a devastating disease that causes severe functional and cognitive decline."

For more information about the BV-101 Huntington's Disease clinical trial, contact *askfirst@askbio.com* or visit *www.askbio.com* or go to: *Clinical Trials Register*

For additional information on this trial, please visit *Landing Page*

MULTIPLE SYSTEM ATROPHY CLINICAL STUDY

The clinical program for Multiple System Atrophy (MSA) has an active Investigational New Drug Application and is preparing to enroll patients in a study (*NCT04680065*) to evaluate the safety and potential clinical effect of AAV2-GDNF delivered to the putamen in patients with a diagnosis of MSA with predominant parkinsonism symptoms. The randomized, controlled study intends to enroll nine patients in the U.S. through The Ohio State University Medical Center, University of California-Irvine and University of California-San Diego.

By enhancing levels of a naturally occurring growth factor, GDNF gene therapy is intended to promote the survival and functioning of vulnerable brain cells that degenerate in Parkinson's disease and MSA. Harnessing the brain's own cellular machinery, GDNF gene therapy provides continuous production of GDNF that may provide an advantage over intermittent protein infusions of synthetic GDNF where levels may be subtherapeutic between infusions.

PARKINSON'S DISEASE AND MULTIPLE SYSTEM ATROPHY RESEARCH STUDY

AskBio is also starting a research study that will be open to patients diagnosed with Parkinson's disease (PD) or MSA. PD patients who are within 1-6 years from their initial diagnosis and MSA patients who are within 4 years of their initial diagnosis may be eligible. The study is designed to determine how PD and MSA change up to an 18-month period by evaluating the following:

- Measurement of blood biomarkers every 6 months and spinal fluid biomarkers at two timepoints
- In-person clinic visits every 6 months
- At-home questionnaires every 3 months

Your participation will be a key factor in growing our understanding of how PD and MSA symptoms and biomarkers change over time, and it will ensure that future studies are designed to better understand the effects of gene therapy.

For questions about participation or other aspects of this study please contact *askfirst@askbio.com* or goto *XXXXX*

AN INTERVIEW WITH PHILIP FORTIER – EXECUTIVE DIRECTOR OF THE DEFEAT MSA ALLIANCE

(L to R): Philip Fortier, Nadia di Lorio, Mattia Fontana, Tiliano Fontana

How has Multiple System Atrophy (MSA) personally affected you?

My entry into the MSA world came with my brother Joe who had MSA. He was diagnosed at 53 and passed away at 56, after a particularly cruel decline. His MSA was confirmed upon autopsy.

My brother Joe had a career in the medical field, managing sleep disorder clinics throughout Southeastern Michigan and helping to conduct sleep research.

The most significant symptom of his MSA was orthostatic hypotension. He had severe drops in BP, when changing positions and after eating. Even while on max doses of the very few BP drugs on the market at the time, he could barely lift his head. He was entirely bedridden, unable to move or to speak.

During his life, I was involved in trying to get droxidopa, a generic medication that showed in promise in treating orthostatic hypotension. Eventually he was able to get the drug via the expanded use process and he benefitted from it for the last 6 months of his life. He was able to relate with his family more and it improved the quality of his life. True, it did not slow the underlying disease, but it helped make his life worth living – it improved the quality of his life. After my brother's death in 2013, I helped in the successful effort to get droxidopa approved by the FDA, testifying on behalf of MSA patients and their families.

Since that time, I have continued to be involved in the MSA cause. With the help of my spouse who is a neurologist, I started Defeat MSA Alliance (USA) in 2013, Defeat MSA/ Vaincre MSA Canada in 2019, Defeat MSA Australia in 2020 and Defeat MSA New Zealand in 2021. Also in 2021, with the addition of 2 other previously formed charities in Spain and Italy, the MSA United Consortium was founded. In 2022, MSA Denmark joined the global consortium.

What lead you to start Defeat MSA Alliance?

Despite having good connections in the medical field, my brother encountered many medical professionals that knew little, if anything, about MSA. And because there was little knowledge, people did not seem to care about this devastating condition. MSA patients are confronted with a dim prognosis and left with few options for treatments. My brother also thought it was important to get the word out there about the lives of people affected by MSA.

How important is it to find new treatments for MSA?

The starting point toward the progress to new treatments begins with awareness, with more awareness comes more support and true support brings with it a concern for effective treatments. Awareness and support are key but there must be real movement toward new treatments. Otherwise, it is just lip service. We must be willing to put our words into action!

What do you wish people knew about living with MSA?

Like any chronic disease, there are challenges in everyday living. But people suffering from MSA have added complications, which are oftentimes not present in other more well-known diseases. There are very few treatments and little knowledge about the condition among the public. The social isolation of having this disease can be overwhelming. We need to increase medical knowledge about MSA while also raising greater awareness among the public.

What are your hopes for the future?

Simply put, my hope is that each person diagnosed with MSA will be afforded a fighting chance to live and flourish, despite the rarity of their condition. That their life will be valued. There is no disease so rare that it does not deserve treatment. I see medical treatment, even for rare and chronic neurodegenerative disorders such as MSA as a human right that needs to be honored and uplifted. We are getting better as a society, recognizing the human toll in the rare disease community but we can do so much more. I am often reminded of a civil rights motto: "if not us, then who, if not now, then when?" This is true of MSA, just as any other serious social ill. We have the moral duty to make the change we want to see, and the time is now to do it.

ASKBIO TECHNOLOGY AND MANUFACTURING

Many great ideas don't reach their full potential in the process of translating them into products – we're all still waiting on flying cars and the final books of the Game of Thrones series. Gene therapy is no different – and as the adeno-associated virus (AVV) technologies that underpin our therapeutics gain more and more momentum, the world is starting to take notice. Lifechanging therapeutics can be developed, but in some cases not scaled up to meet demand leaving patients and families looking at medicine that is out of reach because of supply constraints, cost, or access. Making safe, effective gene therapy medicines is incredibly challenging in its complexity, and for much of the industry the focus was on concept, not what it would take to move forward if the concept worked. For Askbio, though, thanks to long years of work that was in many ways ahead of its time, we can be confident not just in the concept but the full story of development and manufacturing of incredible medicines.

AAV depends on other viruses to be present in order to replicate – a great advantage in terms of safety, but a real challenge when the job is to make as much of it as possible. Through years of research (significant portions of which were done by Askbio's scientific leadership) a number of methods have been developed to create the right conditions for AAV to be produced – some use other viruses, and some methods, like Askbio's manufacturing platform, combine a receptive cell type with the genetic elements AAV needs encoded on linear or circular DNA that are then put inside those cells. AAV virus is then produced, purified, and made ready for the patient. Along the way more than 30 different tests are run to ensure safety and efficacy.

While these manufacturing methods have been well understood for many years, Askbio has been a leader in making our methods ready for patients that need large amounts of AAV. People like our Chief Technology Officer, Josh Grieger, worked to isolate productive cells and put them in growth medias that meet modern standards for manufacturing. Askbio has also developed the best viral helper constructs in the industry, and allowed them to be used by everyone, without a license, in order to help AAV everywhere be more productive. And we're continuing to innovate, optimizing our current methods while developing new ones to continue to keep our leadership position in making gene therapy more safe, more accessible and available at a lower cost.

HOPE TRAVELS

Hope Travels: Hope relaxing in the pumpkin patch, helping to raise Pompe disease awareness on a fine fall day!

UPCOMING MEETINGS:

MDA Clinical & Scientific Conference
Dallas, TX 2/19/23 – 2/22/23

World Symposium
Orlando, FL 2/22/23 – 2/26/23

NEWSLETTER

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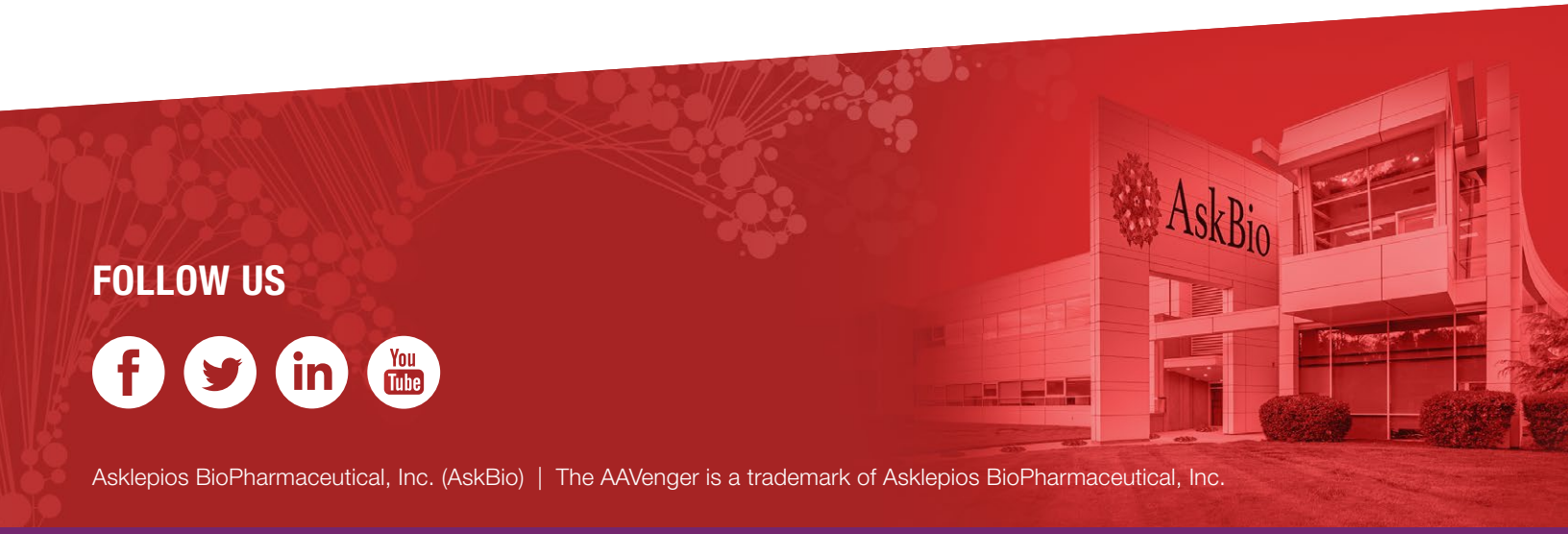

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