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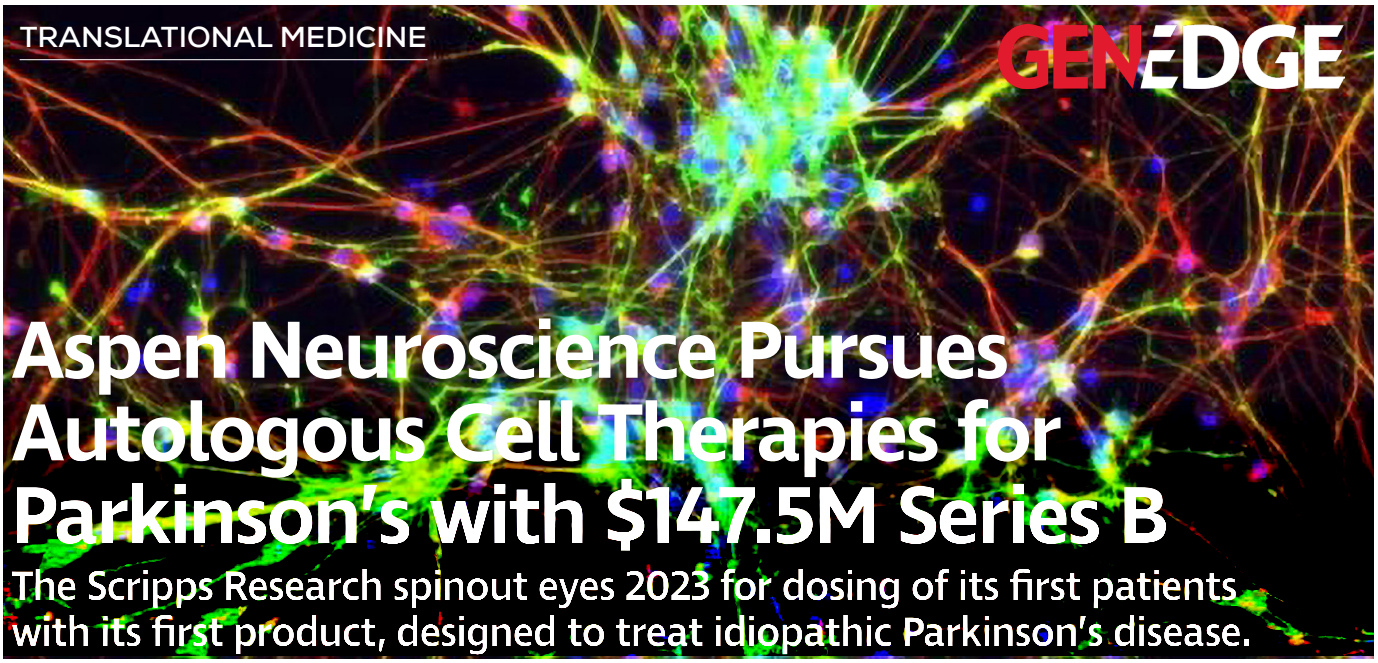

Aspen Neuroscience Pursues Autologous Cell Therapies for Parkinson's with $147.5M Series B

The Scripps Research spinout eyes 2023 for dosing of its first patients with its first product, designed to treat idiopathic Parkinson's disease.

Scripps Research spinout Aspen Neuroscience develops induced pluripotent stem cell (iPSC)-derived dopaminergic neurons from the skin cells of Parkinson's disease patients. The company plans to advance its lead cell therapy candidate for Parkinson's into its first clinical trial next year, using part of the proceeds it raised from the $147.5 million Series B financing it completed earlier this month. [Aspen Neuroscience]

Alex Philippidis

Parkinson's disease (PD) has been a tough nut to crack in terms of developing successful therapies—"extremely challenging" according to a 2020 study, citing limited understanding of the mechanisms of neurodegeneration in PD, the heterogeneity of the pathology, and lack of adequate animal models.

Hence, the interest by some academic researchers and companies in using cell therapy to treat the neurodegenerative disorder, which affects 10 million people worldwide, including almost one million patients in the U.S.

Among companies developing Parkinson's cell therapies is Aspen Neuroscience. The privately-held San Diego biotech plans to advance its lead cell therapy candidate for PD into the clinic next year, using part of the proceeds it raised from a $147.5 million Series B financing it completed earlier this month.

That candidate, ANPD001, is an autologous dopamine neuron replacement therapy derived from induced pluripotent stem cells (iPSCs). The therapy—the first of its kind, according to Aspen—is designed to treat sporadic or idiopathic PD, which accounts for an estimated 85–90% of Parkinson's cases.

Damien McDevitt, PhD,
Aspen Neuroscience President and CEO

Aspen is evaluating ANPD001 in the Trial-Ready Cohort Study launched last month as a preliminary step to filing an Investigational New Drug (IND) application with the FDA. Through the screening study, taking place across multiple clinical screening sites, the company is taking biopsies from 20–30 patients, from which Aspen plans to identify the 10–20 patients who will be assessed further in the Phase I/IIa trial it plans to launch over the coming year.

"We would hope to get the IND filed in the beginning of 2023, and then be able to start dosing our patients in 2023 as well," Aspen President and CEO Damien McDevitt, PhD, told GEN Edge.

By 2024, Aspen plans to enter the clinic with its second candidate for PD, ANDP002 for genetic Parkinson's, an autologous gene corrected therapy now in the research stage.

ANDP002 "is for a subset of Parkinson's patients that have GBA mutations, about eight percent of PD patients. Our concept is to do gene correction on top of the cell replacement: You make the cells, you do the gene correction, and then you make the dopaminergic neurons," McDevitt said. "It's a bit of a longer process than for our idiopathic Parkinson's program. But it's really exciting. It's about a year behind the lead program."

He said Aspen envisions developing two additional candidates as it builds out its pipeline.

Secret sauce

Aspen gathers cells from patients through a skin biopsy. The company uses undisclosed proprietary genomics tools based on machine-learning algorithms to assess patients' iPSC-derived dopamine neurons for potential effectiveness before transplantation into those patients.

"This is part of the secret sauce of Aspen -- how we're able to pick out the best clones," McDevitt said. "It's based on markers on the cells and screening all these markers. We look for many markers in these cells to pick the ones that are predictive of becoming the highest quality iPSC clones, as well as the dopaminergic neurons that are predictive of engrafting and innovating and giving us the best outcomes."

"[We] want to engraft so [the cells] persist in the brain, and then be able to express dopamine. Then [we] want to be able to innovate and clone these neuronal networks," McDevitt continued. "You need all that before you get successful biological effects. We're basically screening for markers that enable those activities."

Aspen says its approach cuts the time and cost of manufacturing needed to produce safe, reproducible, and personalized autologous cell therapies. The company says its in vitro and in vivo studies have shown that its protocol reliably produces dopamine-releasing neurons when examined both physiologically and functionally.

Aspen reasons that its autologous approach to cell therapy holds advantages over allogeneic strategies: No need for immunosuppression, the potential to scale up manufacturing to millions of cells per patient, a reduced probability of mutations due to little cell expansion, and the possibility that patients can be re-dosed.

"What you really want to do is replace and back up the cells so as to have the amount of cells that a healthy individual would have—the 200,000 mark," McDevitt explained. "We believe we've got an advantage over a gene therapeutic approach, where you're fixing cells that are broken. We're actually adding more of the good cells back into the patients. We've got an advantage over small-molecule therapies, where patients have to take L-DOPA every day, and then they struggle with the on-and-off effects of L-DOPA."

"It could be a once-and-done therapy rather than a daily therapy or a therapy that only slows the progression of the disease," McDevitt said. "We are hopeful our single procedure will be potentially once-and-done—you just put in the cells that you need one time, and you get the biological effects."

Scripps Research spinout

Aspen was launched in 2018 by Jeanne Loring, PhD, Professor Emeritus and Founding Director of The Center for Regenerative Medicine at Scripps Research Institute in San Diego. She was joined by a group of scientists from her lab including Andrés Bratt-Leal, PhD; as well as patient advocates from Summit for Stem Cell who saw promise in the Loring lab's early research of the potential benefits of cell replacement for Parkinson's.

Loring's research provided the methods for differentiation of autologous iPSCs into dopaminergic neurons.

"We expect the cost of treating each patient to be high, but no higher than current CAR-T therapies, and as immunosuppression will not be required, the costs of post-transplant care will be far less than for the unmatched cell approaches. If we are successful, the restoration of health to people living with PD will be priceless," Loring observed in 2018 in Stem Cells and Development, a journal published by GEN publisher Mary Ann Liebert Inc.

Loring is a Special Advisor to Aspen's Research & Development Committee, where she advises the company's R&D program and contributes to Aspen's patent portfolio. Bratt-Leal is the company's Senior Vice President, Research and Development.

McDevitt joined Aspen last year after serving as CEO of Akcea Therapeutics. He previously held senior executive roles at

Ionis Pharmaceuticals, Acadia Pharmaceuticals and GlaxoSmith-Kline (GSK).

Aspen is one of numerous companies and academic researchers pursuing cell therapies for Parkinson's. Last month, Jeffrey Kordower, PhD, founding director of the ASU-Banner Neurodegenerative Disease Research Center at Arizona State University, and colleagues published a proof-of-concept study in Nature Regenerative Medicine showing that a group of non-neuronal cells engineered into functioning neurons effectively reversed motor symptoms resulting from the destruction of dopaminergic cells in Parkinson's disease when implanted in the brains of rats.

Korwoder will serve as principal investigator for a future clinical trial in humans with Parkinson's who bear a mutation in the gene parkin. Those patients do not suffer form cognitive decline or dementia but do suffer from typical symptoms of motor dysfunction found in idiopathic, Parkinson's.

"If you treat and culture them for 17 days, and then stop their divisions and differentiate them, that works best," Kordower said in a statement. "We cannot be more excited by the opportunity to help individuals who suffer from this genetic form of Parkinson's disease, but the lessons learned from this trial will also directly impact patients who suffer from sporadic, or non-genetic forms of this disease."

Kordower added: "Patients with Huntington's disease or multiple system atrophy or even Alzheimer's disease could be treated in this way for specific aspects of the disease process."

Last year, a research team led by Marina E. Emborg, MD, PhD, and Su-Chun Zhang, MD, PhD, both of the University of Wisconsin-Madison, published a study in Nature Medicine showing that monkeys with Parkinson's who received grafts of dopamine neurons grown from their own cells into their brains showed relief from motor and depression symptoms associated with the disease over a two-year period without immunosuppression.

"These behavioral improvements were accompanied by robust grafts with extensive DA [dopamine] neuron axon growth as well as strong DA activity in positron emission tomography (PET)," the research team added.

The world's first clinical trial in humans of an iPSC-derived cell therapy for PD was launched in 2018 by Jun Takahashi, MD, PhD, of Kyoto University, who recently succeeded Nobel laureate and iPSC discoverer Shinya Yamanaka, MD, PhD, as director of the university's Center for iPS Cell Research and Application. Takahashi and colleagues implanted the iPSC-derived precursor cells into the brains of patients, where the cells matured into dopamine-producing neurons.

Last year, Takahashi and colleagues began a limited clinical trial designed to assess potential side effects of iPSC implantation. The trial—which was no longer recruiting patients as of January 2022—was funded in part by Sumitomo Dainippon Pharma, which has committed to pursuing early approval in Japan, with the goal of starting to manufacture and market the cell therapy by next year.

Also among companies pursuing cell therapies for Parkinson's is BlueRock Therapeutics, a cell therapy developer acquired by Bayer for up to $600 million in 2019. BlueRock kicked off 2022 by dosing its first patient in an ongoing Phase I trial (NCT04802733) designed to assess the safety, tolerability, and preliminary efficacy of DA01 in Parkinson's patients one year following cell transplantation.

14.9% Success rate

A study published last year illustrates the difficulty of developing PD treatments: The FDA has approved only 15 drugs for PD indications since 1999, for an overall success rate of just 14.9%--much higher than Alzheimer's (<1%) and Huntington disease (3.5%), and higher than neurological diseases in general (9%), but lower than cancer (about 19%).

"The good news is that there's a number of different approaches here. That's great for patients, and it's great for the cell therapy space," McDevitt said. "We're excited to learn from other studies. It'll help us as we progress our study. But we're pretty advanced, and we're pushing towards getting our IND filed and approved over the next year or so and getting into the clinic."

Aspen is also working toward expanding its workforce, which has grown from 23 people when McDevitt joined the company, to about 65 people today. The company plans to build out its manufacturing and QA/QC teams, as well as fill specific C-suite positions. The company is currently recruiting a chief technology officer and McDevitt says "we will probably be looking for a general counsel" with an eye on becoming a public company down the road. "By the end of the year, we'll grow to about 90 people."

As a smaller company, Aspen is staying focused on PD, although it is open to partnering at least some of its programs, drawing on McDevitt's background in business development and partnerships at previous companies. "Business development is a critical part of the strategy of the company. How do we grow a pipeline in a very sensible way with partners? Hopefully we'll be able to announce something on that in the future."

Aspen's Series B financing was in the works for "about seven or eight months," starting late last year. The financing took a little longer to complete than anticipated due to the biopharma bear market of recent months, though McDevitt noted, "We were able to raise the high end of our range."

The new financing brings to more than $220 million the total capital raised by Aspen. The company completed a $70 million series A round last year and emerged from stealth mode after raising $6.5 million in seed financing in December 2019.

Aspen's Series B was co-led by GV (formerly Google Ventures), LYFE Capital, and Revelation Partners, with participation from additional new investors Newton Investment Management, Singapore-based government linked global investment fund EDBI, LifeForce Capital, Medical Excellence Capital Partners, Mirae Asset Capital, NS Investment and others.

The financing round included significant investments from investors that participated in Aspen's Series A and Seed rounds—including OrbiMed, ARCH Venture Partners, Frazier Life Sciences, Section32, and Alexandria Venture Investments.

As part of the Series B, Doug Fisher, MD, a Partner with Revelation Partners, will join Aspen's board. "We were excited that there was a lot of interest in the story, the company, the technology, the team, and the intellectual property in the company," McDevitt said. "And we were very excited about the outcome!" GEN