4DMT and Arbor Biotechnologies Establish Partnership to Co-Develop and Co-Commercialize Next-Generation Genetic Medicines for CNS Diseases

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- *Partnership brings together two leaders in next-generation genetic medicines to engineer, co-develop and co-commercialize (50:50 profit share) AAV-delivered CRISPR/Cas-based therapeutics for up to six product candidates in CNS*
- *Initial product candidate will be developed for a target in amyotrophic lateral sclerosis (ALS) with additional targets expected to be in diseases with high unmet need in both rare and large patient populations*
- *4DMT to contribute both 1) its customized AAV vectors targeting various CNS tissues, invented through its proprietary Therapeutic Vector Evolution platform, and 2) its robust AAV product development engine*
- *Arbor to contribute both 1) its proprietary AAV-compatible modular toolbox of gene editing technologies, compact enough to allow cargo insertion into a single AAV product, and 2) its CNS therapeutic area expertise*

EMERYVILLE, Calif. And CAMBRIDGE, Mass., Jan. 03, 2024 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT, 4DMT), a leading clinical-stage genetic medicines company focused on unlocking the full potential of genetic medicines to treat large market diseases, and Arbor Biotechnologies, Inc. (Arbor), a next-generation gene editing company developing potentially curative therapeutics for patients with serious diseases based on its proprietary and modular toolbox of DNA-editing technologies, today announced a strategic partnership focused on advancing new AAV-based gene-editing therapies for central nervous system (CNS) diseases with high unmet medical needs in both rare and common disease populations. 4DMT and Arbor will co-develop and co-commercialize up to six AAV-delivered CRISPR/Cas-based therapeutic candidates, with the costs and profits shared evenly based on mutually agreed plans.

Arbor will lead research, development and, if approved, commercialization efforts on the first product candidate in the collaboration, which will address a molecular target implicated in amyotrophic lateral sclerosis (ALS). 4DMT will lead research, development and, if approved, commercialization efforts on the second product candidate (target and disease to be disclosed at a future date).

Arbor utilizes its artificial intelligence and machine learning, or AI/ML, driven discovery engine and protein engineering capabilities to identify and optimize genomic editors with the potential to treat a broad range of genetic diseases. Arbor's proprietary portfolio of novel genomic editors has therapeutic potential due to, among other things, their unique cut patterns and protospacer adjacent motifs (PAMs). The PAMs, for example, may enable Arbor to access greater than 93% of all sites in the human genome which allows it to target nearly any genetic locus. The small size of Arbor's genomic editing technology allows the use of additional delivery mechanisms with their high specificity, which can enable improved safety profiles. Arbor also has expertise in CNS biology, CNS drug development and CNS therapeutic development.

4DMT's proprietary invention platform, Therapeutic Vector Evolution, has yielded customized and evolved, highly targeted AAV vectors in ophthalmology, pulmonology and cardiology that have demonstrated differentiation compared to naturally occurring AAVs in clinical studies. Initial evidence includes strong clinical activity in wet age-related macular degeneration (wet AMD) with low dose, intravitreal delivery using the R100 vector (4D-150 product candidate), and unprecedented transgene expression was achieved in the lungs of people with cystic fibrosis using the A101 vector (4D-710 product candidate). 4DMT has utilized its platform to invent customized AAV vectors for CNS tissues, and these vectors will be deployed in the partnership. In addition, the partnership will leverage 4DMT's AAV product design and engineering, manufacturing, clinical and regulatory development expertise.

"CNS disorders include some of the most devastating diseases, many of which have a genetic origin. The technology to effectively edit the underlying genetic mutations within these diseases did not exist until an AAV compatible genomic editing technology was developed. Utilizing our expansive toolbox of AAV compatible genomic editors, we aim to advance the development of potential lifesaving therapies for CNS diseases, and we're delighted to partner with 4DMT as a part of this mission," said Devyn Smith, Ph.D., Chief Executive Officer of Arbor. "4DMT's proprietary, customized and evolved AAV vectors potentially provide the best delivery vehicles for our gene editing payloads to target select regions of the brain that we believe could provide meaningful benefits to patients in both rare and large CNS patient populations."

"The recent landmark FDA approval of the world's first CRISPR-based treatment is a revolutionary event for genetic medicines and the biotech industry. Gene editing technology continues to rapidly advance and we believe the safe and efficient delivery of these potentially transformative therapies can address CNS diseases of high unmet need," said David Kirn, M.D., Co-Founder and Chief Executive Officer of 4DMT. "Arbor is at the forefront of this rapid innovation, and they have discovered and optimized gene editing payloads that are compact enough to be delivered within a single AAV vector. We look forward to combining our complementary technologies and capabilities to power a new generation of potential genetic medicines. This collaboration provides us with the opportunity for next-generation gene editing capabilities and CNS products, while simultaneously allowing us to maintain our focus on clinical development in large market ophthalmology and pulmonology."

About Amyotrophic Lateral Sclerosis

ALS, often called Lou Gehrig's disease, is a progressive neurodegenerative disease in which the motor neurons atrophy and die, resulting in loss of the ability to speak, move, eat and, eventually, breathe. ALS is typically fatal within approximately two to five years of symptom onset. The disease is estimated to impact approximately 79,000 people in the United States, EU, and UK. There are multiple approved treatments available for ALS and its symptoms, but there currently is no cure.

About Arbor Biotechnologies

Arbor Biotechnologies® is a next-generation gene editing company based in Cambridge, MA. Combining the promise of CRISPR with advanced computational AI-driven discovery, high-throughput screening, and robust protein engineering approaches, our scientific co-founders Feng Zhang and David Walt laid the groundwork for our proprietary discovery engine, that has yielded an extensive portfolio of novel genomic editors. We envision a future of gene editing that extends beyond simple knockdowns to include reverse transcriptases, nuclease excisions and large insertions. This affords

us the potential to treat a broad spectrum of patients, from those with ultra-rare to the most common genetically defined diseases. Guided by a deep understanding of the molecular basis of disease and our access to a unique suite of optimized genomic editors, we are rapidly advancing our development programs with an initial focus on genetically defined liver-mediated and CNS diseases. As we advance toward the clinic with our first therapeutic candidate in primary hyperoxaluria type I, we look to expand our strategic partnerships around in vivo genomic editing across multiple therapeutic areas and ex vivo cell therapy programs to broaden the reach of our novel gene editing technologies. For more information, please visit: arbor.bio.

About 4DMT

4DMT is a leading clinical-stage genetic medicines company focused on unlocking the full potential of genetic medicines to treat large market diseases in ophthalmology and pulmonology. 4DMT's proprietary invention platform, Therapeutic Vector Evolution, combines the power of the Nobel Prize-winning technology, directed evolution, with approximately one billion synthetic AAV capsid-derived sequences to invent customized and evolved vectors for use in our wholly owned and partnered product candidates. Our product design, development, and manufacturing engine helps us efficiently create and advance our diverse product pipeline with the goal of revolutionizing medicine with potential curative therapies for millions of patients. Currently, 4DMT is advancing five clinical-stage and two preclinical product candidates, each tailored to address rare and large market diseases in ophthalmology, pulmonology, and cardiology. In addition, 4DMT is also advancing programs in CNS through a gene editing partnership. 4D Molecular Therapeutics™, 4DMT™, Therapeutic Vector Evolution™, and the 4DMT logo are trademarks of 4DM.

All of our product candidates are in clinical or preclinical development and have not yet been approved for marketing by the FDA or any other regulatory authority. No representation is made as to the safety or effectiveness of our product candidates for the therapeutic uses for which they are being studied.

Learn more at www.4DMT.com and follow us on LinkedIn.

4DMT's Forward Looking Statements:

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding the therapeutic potential, abilities, safety and efficacy of 4DMT's CNS vectors, including in connection with Arbor's use thereof pursuant to the Collaboration Agreement, the potential benefits or applications of 4DMT's Therapeutic Vector Evolution platform, including any other vectors developed through the Therapeutic Vector Evolution platform, and the amount of potential payments under the Collaboration Agreement. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including risks and uncertainties that are described in greater detail in the section entitled "Risk Factors" in 4D Molecular Therapeutics' most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 4D Molecular Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. 4D Molecular Therapeutics explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward looking statements.

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