EMERGING COMPANY PROFILE

HARNESSING AAV TROPISMS

BY VIRGINIA LI, STAFF WRITER

Bamboo Therapeutics Inc. is developing adeno-associated viral vector-based gene therapies that preferentially target tissues affected by CNS and neuromuscular disorders. By homing in on specific tissues, Bamboo’s gene therapies could minimize off-target toxicities and reduce the amount of virus needed to produce a therapeutic effect.

The newco spun out of gene therapy company Asklepios BioPharmaceutical Inc. last year with an initial focus on BMB-D001, a systemic gene therapy for Duchenne muscular dystrophy designed to produce a functional form of dystrophin specifically in tissues where it is needed.

The program employs the AAV serotype 9 (AAV9) vector, which displays a natural tropism toward cardiac and skeletal muscle, and delivers a functional “mini-dystrophin” gene that has been truncated to 4.6 kb. That allows it to fit within AAV packaging capacity, said CEO Sheila Mikhail, and gets around the problem that the full 2.4 Mb dystrophin gene is too large for AAV vectors. Bamboo has exclusive, worldwide rights to AAV9 from GlaxoSmithKline plc for neuromuscular indications.

DMD is caused by nonsense mutations in the dystrophin gene, and the most advanced therapies involve strategies to bypass mutations, allowing cells to produce a functional dystrophin protein. By using gene therapy, Bamboo is shooting for a potential cure.

There are no approved DMD therapies in the U.S., while PTC Therapeutics Inc.’s Translarna ataluren is conditionally approved in Europe for ambulatory nonsense mutation DMD patients aged five and older. The compound facilitates complete translation of dystrophin containing nonsense mutations.

According to Mikhail, yet-to-be published data from a golden retriever model of DMD show BMB-D001 led to long-term expression of a functional form of dystrophin, allowing for walking eight years after treatment. The program was begun at Asklepios.

The company plans to begin a Phase I trial in 2H16 of BMB-D001, which will be administered as a single IV injection. The trial will enroll 9-18 patients and evaluate improvements from baseline on clinical outcomes including six-minute walk distance (6MWD) and the North Star Ambulatory Assessment (NSAA).

Solid Biosciences LLC’s Solid GT subsidiary is also developing a DMD gene therapy that will deliver a shortened version of the dystrophin gene using an undisclosed vector. The therapy is expected to enter the clinic in 2017. Mikhail declined to compare its approach to Solid’s.

Bamboo’s pipeline also includes therapies for giant axonal neuropathy (GAN), Friedreich’s ataxia and Canavan’s disease.

scAAV/Jeg-GAN, an AAV9 vector encoding the gigaxonin gene, is in an NIH-sponsored Phase 1/II study to treat GAN with data expected mid-2018. Gigaxonin targets proteins for destruction by the ubiquitin-proteasome system, and mutations to the gene lead to the abnormal accumulation of neurofilaments in nerve cells that characterizes GAN. Mikhail said scAAV/Jeg-GAN is administered intrathecally, allowing for efficient distribution within the CNS.

Bamboo is also developing a chimeric vector that delivers the frataxin (FXN; FRDA) gene to treat Friedreich’s ataxia. The disease stems from low levels of frataxin, which leads to degeneration of the nervous system and subsequent cardiac disease and stroke-like symptoms. Mikhail declined to disclose details regarding the vector, but said it preferentially delivers frataxin to the brain and heart. The candidate is slated to enter the clinic in early 2018.

The company’s program for Canavan’s disease uses an undisclosed vector that targets oligodendrocytes and delivers the gene for aspartoacylase. Canavan’s is characterized by impaired brain development resulting from decreased levels of aspartoacylase. Bamboo has exclusive, worldwide rights to the Canavan’s therapy from Rowan University. Mikhail said the company’s program could provide proof of concept for a vector that could be used to target oligodendrocytes in larger indications, such as amyotrophic lateral sclerosis (ALS) and Alzheimer’s disease (AD).

Bamboo closed a $49.5 million series A round in January that included participation from CureDuchenne Ventures LLC, the venture arm of CureDuchenne. Asklepios also holds an undisclosed equity stake in the newco.

Mikhail said the round will enable Bamboo to complete Phase I trials of its DMD and Friedreich’s ataxia candidates, after which Bamboo may seek development and commercialization partners.

COMPANIES AND INSTITUTIONS MENTIONED

Asklepios BioPharmaceutical Inc., Chapel Hill, N.C.
Bamboo Therapeutics Inc., Chapel Hill, N.C.
CureDuchenne, Newport Beach, Calif.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
National Institutes of Health (NIH), Bethesda, Md.
PTC Therapeutics Inc. (NASDAQ:PTCT), South Plainfield, N.J.
Rowan University, Glassboro, N.J.