

Company Spotlight

LONGEVITY APPLIES INNOVATIVE PLATFORM TO CNS BIOLOGICS

Longevity Biotech is a privately held company based in Philadelphia with a unique platform technology that combines the features of biologics and small molecules to create a new class of therapeutic compounds. NeuroInsights spoke with Dr. Scott Shandler, co-founder and CEO, to learn more about the ongoing projects and future plans for the company.

Longevity was formed in 2010 around nascent technology out of University of Wisconsin from Dr. Samuel Gellman's academic lab. Gellman is a leader in "foldamers", which are synthetic structures that adopt various conformations and with that, specific functions. He developed a method to incorporate non-natural amino acids into biological peptides to improve the product profile, including protease resistance and shape stability.

Shandler connected with Gellman through their scientific network. "We went for sushi in Madison, Wisconsin on July 4, 2010, and talked all about science," comments Shandler, who was excited about the possibilities that the technology represented. Longevity licensed several families of patents from University of Wisconsin that covered the platform technology, *Hybridtides*. The company moved into the University City Science Center, an incubator in Philadelphia, in 2011 and is developing and incorporating the technology into a variety of preclinical programs.

The *Hybridtide* technology changes the stability of the peptide as it shifts the geometry of the molecule that it is applied on. Some of the pathways involve a combination of alpha-amino acid residues with beta-amino acid residues, to generate alpha/beta-peptides. This, in turn, limits the ability of proteases to cleave peptide bonds efficiently and break molecules into smaller pieces. The resulting peptide or molecule is still degraded but at a rate that is several orders of magnitude slower. Shandler shares, "There are a couple of key features we are excited about, including the prospect of oral delivery for these compounds. It is a tall mountain to overcome but the oral delivery of these molecules will change the landscape of therapeutic opportunity." The surfaces of the molecule are preserved, and hence the functional components retain native activity. Shandler continues, "The analogy I like to use is crude, but essentially we stick a steel rod through the interior of the molecule, and that allows us to structurally and digestively stabilize the molecule."

A couple other interesting facts about the platform are that the changes that are made are connected to changes in signal propagation. Shandler describes the concept of "Artisan

BiologySM", meaning that they are able to customize the biological signaling cascades, taking advantage of unique structural attributes that result in signal bias. This is a result of newer platform capabilities and has the potential to remove side effects of a given pathway. In addition, because of the protease resistance it may be possible to overcome immunogenicity problems that often arise for conventional peptide drugs. This would have a significant impact on the way peptide therapeutics are developed, and Longevity is positioned to be the leader in this area.

Longevity is currently focusing on an immunomodulatory asset that can be applied to Parkinson's disease (PD) but also has potential in other CNS disorders, as modulating neuroinflammation would be therapeutically relevant in a number of indications. The company is collaborating with Dr. Howard Gendelman from University of Nebraska in the PD indication. Acute studies in the MPTP mouse model have demonstrated remarkable neuroprotective ability of Longevity's vasoactive intestinal peptide receptor 1 and 2 (VPAC) *Hybridtide* agonists *in vivo*. In addition, VPAC agonists have an influence on both innate and adaptive immunity, both of which have been linked to progressive nigrostriatal degeneration in PD. Results from the preclinical studies with peripheral administration demonstrate protection of tyrosine hydroxylase neurons, reduced microglia reactivity, and downregulation of pro-inflammatory cytokines, suggesting a phenotypic shift of T cells to neuroprotection. Studies are also investigating the ability of this candidate to cross the blood brain barrier. Longevity is preparing to carry out IND-enabling studies and hopes to be in the clinic with their neuroscience program in the next 12 to 24 months.

In addition, Longevity has a varied pipeline in HIV, diabetes, cardiovascular and oncology indications. All the assets are scientifically connected in that the targets pursued are cell-surface receptors or protein-protein interaction targets that can be addressed by a peptide. In these efforts they have been quite successful, for example the viral fusion inhibitor *Hybridtide* has been improved with respect to the original compound, as the application of the platform has increased the stability 300x while maintaining the potency and function of the compound. The Type II diabetes program has already been partnered and is also advancing rapidly.

Longevity was one of the inaugural recipients of the Thiel Foundation's Breakout Labs funding in 2012. Shandler comments, "Breakout Labs appreciates platforms with a big human health impact." He points out that the Foundation is very supportive at every step of the way and that the grant recipients have become very close and help each other with diverse operational issues. In addition, the company recently received funding from NetScientific in 2014. Sir Richard Sykes, previously Chairman and CEO at GSK, currently heads NetScientific. Hence, Longevity has received an international vote of confidence and has a global

syndicate of investors. At present, Longevity is raising a Series A and has received strong investor interest.

Longevity is open to many options in terms of collaborations and partnerships. Companies interested in applying the *Hybridtide* platform to their assets could benefit from an early stage partnership that improves their product profile while maintaining control of clinical development. In other cases, Longevity is looking to partner some of their assets for clinical development. The company also remains open to academic collaborations. 
