Emerging Company Profile

Coferon: Some assembly required

By Michael Flanagan
Senior Writer

Rather than trying to make ever smaller molecules that retain activity against complex targets, **Coferon Inc.** is using a bioorthogonal linker technology to deliver two halves of a therapeutic that self-assemble on the target after gaining entry into a cell. The company was set to announce the close of a $12 million series B round on Monday this week.

Targeting intracellular protein-protein interactions requires walking a fine line — a therapeutic needs to be small enough to enter the cell but large enough to modulate the interface between two bulky proteins.

One way to do so is to use macrocycles, which feature a ring structure adorned with functional subunits. These typically range in size from 500-2,000 Da., making them larger than most small molecules but smaller than biologics *(see "Ra Materials," A13 & "Mini-Macrocycle Marriage," A15)*.

Coferon is taking a new approach that it hopes will allow for better potency and selectivity than agents like macrocycles because there will be less need to decrease target coverage to optimize an agent's ADMET properties, according to Chairman and CEO Colin Goddard. It also should be amenable to a wider range of targets by allowing for delivery of larger post-assembly agents.

The company's reversible covalent linker chemistry was invented together by groups at **Weill Cornell Medical Institute** and **Purdue University** and is exclusively licensed to Coferon.

The strategy is to take a therapeutic that is too bulky for oral delivery or cell permeability and split it into two smaller components.

The technology first links the two chemically synthesized monomers, which dissociate under physiological conditions inside the body so that they are small enough to cross the cell membrane. Once inside the cell, the linker moieties engineered onto each monomer dimerize using the macromolecular binding site as the template.

"The molecular weight of each of the monomers is 500-700 Da, so we can double the binding footprint and offer better selectivity, specificity and potency," said Goddard.

Coferon has patent applications pending related to the linker technology and will seek composition of matter patents for each individual candidate.

Coferon Inc.

New York, N.Y.

Technology: Small molecule monomers that self-assemble intracellularly

Disease focus: Autoimmune, cancer, infectious disease

Clinical status: Discovery

Founded: 2009 by Francis Barany, Donald Bergstrom, Maneesh Pingle and Derek Small

University collaborators: Weill Cornell Medical Institute, Purdue University, Stony Brook University

Corporate partners: None

Number of employees: 5

Funds raised: $19 million

Investors: Hatteras Venture Partners; MedImmune Ventures; Ascent Biomedical Ventures; Morningside Group; and angel investors

CEO: Colin Goddard

Patents: None issued

The company picked up the technology at the concept stage in 2009, and according to Goddard, achieved its first proof of principle this year by showing dimers were able to inhibit beta tryptase in human mast cells in both cellular and mouse models. Coferon plans to publish the data within 12 months.

Both homodimeric pairs and heterodimeric pairs were shown to work, he added.

"Proving in live cell assays and *in vivo* mouse models that the technology actually worked was the driver that allowed us to attract our new investors," said Goddard.

Although beta tryptase was ideal for showing monomers can be delivered to target mast cells where dimerization and target inhibition occurs, Goddard said the clinical utility of that pathway has not been validated. Thus, the company has no plans to move the program into the clinic.

Coferon instead is concentrating on two discovery projects. One is an epigenetic program focused on the bromodomains of the BET family of proteins, with a primary target of bromodomain containing 4 (BRD4), which has been validated in mouse models in immunology and oncology.

The BET bromodomains monitor histone acetylation — the reverse process of histone deacetylation — and act to regulate gene expression by helping to control when and what portion of DNA is exposed by the chromatin structure.

The proteins were considered undruggable because they do not possess enzymatic activity until a pair of groups reported in 2010 the discovery of a small molecule BET inhibitor *(see SciBX: Science-Business eXchange, Aug. 11, 2011)*.

The other program is addressing an undisclosed infectious disease target.

Coferon hopes to find a partner for the bromodomain project and wants to carry the infectious disease program through Phase II testing before seeking a partner.

Investors in the company's $12 million series B round include Hatteras Venture; MedImmune Ventures; and Ascent Biomedical.

The money should provide Coferon with 12-18 months of runway, "which should let us reach the candidate generation stage with two or three targets and furnish one significant partnership in the epigenetic space," Goddard said.

Prior to this week, Coferon had raised about $7 million via multiple closes of a series A round from angel investors and Morningside.

COMPANIES AND INSTITUTIONS MENTIONED

Coferon Inc., New York, N.Y.
Purdue University, West Lafayette, Ind.
Weill Cornell Medical Institute, New York, N.Y.