Roundabout Therapeutics

FOUNDING TEAM

Fred Ausubel, PhD - Distinguished professor with decades of research into host-microbe interactions
Shen (Peter) Yu, PhD - Microbiologist and inventor with crystallographic expertise
Isaac Stoner - Entrepreneur with experience developing and commercializing complex biological products
Paul Goldenheim, MD - Experienced executive with deep expertise in drug development and anti-infectives
Erik Vogan, PhD – MIT Industry Liaison officer

Multi-drug resistant infections in both the hospital and community settings have reached crisis proportions. Nearly 2 million patients will contract one of these infections each year, resulting in high morbidity, extended hospital stays, and patient deaths. MDR infections kill more people per year in the US than breast cancer and prostate cancer combined. New compounds with novel antibiotic mechanisms are desperately needed to combat this growing problem.

Many legacy compounds, as well as new best-in-class broad spectrum agents, are based on beta-lactam derivatives. Strains resistant to these drugs are typically observed in 2-4 years, limiting the value of these iterative compounds.

Through careful study of the basic processes in resistant bacteria, Roundabout has discovered a conserved metabolic pathway that contributes to bacterial pathogenicity. Targeting this pathway affects virulence factors involved in pathogen infectiveness. This metabolic targeting approach can also be used in synergistic combination with other therapeutics to improve outcomes and reduce resistance evolution.

Years of research in the academic setting has created the technical foundations for Roundabout. The team has designed a novel screen and identified two compounds that demonstrate activity against our target pathway. These are both known compounds that have not previously been used as anti-infectives and their use will be protected.

The image below demonstrates the observed efficacy of one experimental compound against a pan-resistant strain of Pseudomonas aeruginiosa (PA14) in a *C. elegans* model of infection. In this infection model, both Roundabout compounds demonstrate superior performance tobramycin, a best-in-class aminoglycoside with $445M in annual sales. Roundabout has screened approximately 10,000 known bioactive molecules, as well as 5,000 novel purified natural products from an academic collaborator. We plan to keep on screening commercially available small molecule libraries up to 400,000 compounds. Screening natural compounds is especially exciting, as most effective antibiotics are based on naturally occurring compounds. Roundabout will protect the results of this screen as well as the screening methodology.

In parallel, Roundabout is performing IND-enabling studies in a mouse model of infection and will evaluate the performance of our lead development candidates against three pathogenic species: *Pseudomonas*, *Acinetobacter*, and *MRSA*.

Antibiotic space has long been characterized by a development void in large biopharma. This creates an opportunity for small innovative drug developers. A changing reimbursement landscape for curative therapies, combined with penalties under the Affordable Care Act are dictating higher price points for anti-infectives. Daptomycin (Cubist) currently receives a $1,200 per course of treatment. This is just $2 per QALY. Other anti-infective therapies such as those for HCV are now receiving reimbursement of more than $41 per QALY*. Even as pressure is being applied by regulators to reduce the cost of prescription pharmaceuticals, public incentive programs are being enacted to spur anti-infective innovation through streamlining regulatory approval and lengthening market exclusivity (GAIN Act, 2012) and providing additional inpatient reimbursement payments for antibiotics associated with high morbidity/mortality infections (DISARM Act, 2015).

Roundabout is developing an anti-infective platform that addresses a multi-billion dollar opportunity in treating multi-drug resistant infection.