GATEWAY BIO, INC.

EXECUTIVE SUMMARY

GATEWAY BIO

A new **WAY** to Conju**GATE**

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Founding Team:

Ashutosh Chilkoti, Ph.D.
- Experienced entreprenuer and founder of PhaseBio (multiple targets in Phase II trials and 65 million in venture capital), and Sentilus (IVD company acquired by Immucor in 2014)
- Expert in drug delivery and principal inventor of Gateway Bio technology
- Professor and Head of Department, Biomedical Engineering, Duke University

Angus Hucknall, Ph.D.
- Co-founder/CEO of Sentilus, which commercialized POEGMA polymer brush technology for in vitro diagnostic use (acquired by Immucor).

Mission: To develop and apply an innovative "PEG-like" drug conjugation technology that eliminates the antigenicity issues surrounding current PEGylation technology.

Problem: Covalent conjugation of therapeutic molecules with the "stealth" polymer poly(ethylene glycol) (PEG), termed PEGylation, is a widely used approach to increase the circulation half-life and reduce the immunogenicity of drugs. Although PEG has been touted as an inert and biocompatible material, recent studies have shown that PEG itself is immunogenic. Current estimates suggest that ~50% of the US population has pre-existing antibodies to PEG, likely caused by chronic exposure to PEGs present in commonly used consumer products. Anti-PEG antibodies lead to accelerated clearance and decreased clinical efficacy of PEGylated drugs, while also increasing the risk and severity of allergic reactions to these drugs. High levels of pre-existing anti-PEG antibodies have recently been linked to serious first-exposure allergic reactions to a PEGylated RNA aptamer, which led to early termination of a Phase III clinical trial. Although PEGylation remains a widely used technology, it is now of great clinical and commercial relevance to develop strategies to deal with the antigenicity and immunogenicity of PEG.

Solution: Our patented POEGMA polymer brush technology has been shown to confer the same drug delivery advantages of traditional PEG conjugates, while simultaneously eliminating anti-PEG antigenicity. We have shown that POEGMA, which breaks up the long sequences of repeating ethylene glycol units found in PEG and presents much shorter oligo(ethylene glycol) sequences, does not interact with anti-PEG antibodies. We have optimized the length of these short ethylene glycol sequences to maximize drug delivery advantages, while eliminating the negative effects of anti-PEG antigenicity. The key to our patented technology is that it exploits a "sweet-spot" in ethylene glycol chain length—we are able to preserve PEG-like properties, while eliminating antigenic PEG epitopes by reducing the number of consecutive ethylene glycol repeat units below a threshold level.

Company Info: Gateway Bio was specifically formed to translate several scientific breakthroughs from the lab of Professor Chilkoti at Duke University into commercially viable products and processes by combining the expertise of the academic scientists closest to these technologies with the business acumen of experienced start-up professionals.

Intellectual Property: The initial core technology of Gateway Bio is based on several key patents on POEGMA conjugates that have been successfully licensed from Duke by Gateway Bio. Gateway Bio currently holds two granted patents: (1) US 8497356 B2 "Biomolecule polymer conjugates and methods for making the same", and (2) US 20160122451 A1 "Enzyme-catalyzed synthesis of site-specific and stoichiometric biomolecule-polymer conjugates". Gateway also holds patent application No. 62/407,403 "Polymer Conjugates Having Reduced Antigenicity and Methods of Using the Same".

Market: Our novel method of creating PEG-like conjugates could be applied to generics, existing drugs, newly developed drugs or any of the PEGylated pharmaceuticals currently on the market. There are currently 15 FDA-approved peglyated drugs, with dozens more in clinical trials. Sales of the two most successful pegylated products, Pegasys and Neulasta, exceeded $5 billion in 2011.

Funding: The technology is currently being developed with the following support, totaling $638,977: (1) MedBlue Incubator Seed Funding $75,000. (2) 2016-BIG-6523 (Chilkoti) Project Period: 9/1/16-2/28/18 NCBC $41,223 "Non-immunogenic PEG conjugates of Biologics". (3) 2016-TEG-1506 (Chilkoti) Project Period: 10/1/16-9/30/17 NCBC $75,000 "Assessing the Manufacturability of a "Next-Gen" Non-Immunogenic PEG-like Conjugate". (4) 2016-Coulter (Hucknall) Project Period: 8/1/16-7/31/17 $170,624 "Next-Generation Non-Immunogenic PEG-like Protein Conjugates" (5) Pending: STTR $277,130.00 Development of a POEGMA-Aptamer rapid onset anticoagulant that eliminates antigenicity to anti-PEG antibodies