A Technology for Improving Biologics Production: Enhancing Glycoprotein Sialylation using Novel Sialidase Inhibitors

The Business Opportunity

One of the biggest challenges facing therapeutic protein production in mammalian cell culture is the unwanted removal of sialic acids from the therapeutic glycoprotein of interest (1). This is due to the actions of mammalian sialidases that are released into the culture medium during production. This loss of sialylation significantly reduces the biological half-life and function of the glycoprotein product thereby reducing the QUALITY of the therapeutic. Also, due to this loss of sialylation the cell growth must be cut short, thereby significantly reducing the QUANTITY of the therapeutic produced per batch. We propose to use our patented engineered compounds to prevent/reduce sialidase activity during Biologics production thereby significantly improving the QUALITY and QUANTITY of each Biologic. Our technology has many advantages, identified below, and should be far-superior to others, such as a sialidase gene silencing approach (1).

A) our technology could be used in ANY mammalian Biologics production platform (ie no cell engineering required), increasing the market size
B) our technology would not alter the properties of the existing Biologic, aside from enhanced sialylation, eliminating possible downstream complications (ie no further clinical trials required).
C) our technology would only be used during Biologics production, and so would be removed during Biologics purification along with any possible unwanted side-effects.

So far, there are no inhibitors that target mammalian sialidases significantly greater than the sialic acid 2-ene compound (DANA), so patented compounds with these properties would hold tremendous business opportunities.

The Technology

Our technology comprises patent protected 2-ene compounds, derived from naturally occurring bacterial sialic acid analogs (2,3). Preliminary testing of only a few of our 2-ene compounds has determined their effectiveness at inhibiting mammalian sialidases, where we observe similar inhibition to that seen with DANA – even before any chemi-enzymatic optimizations. To note, several of our compounds are amenable to chemical derivatization, which will facilitate further product development. This technology not only comprises patented compounds (4), but also includes a patent protected method for the efficient/economical production of sialidase inhibitors from precursor compounds (4), as well as patent protected biosynthetic pathways (5) and cell-based production methods (6) for precursor production. Importantly, these added features may be harnessed for the development of superior mammalian sialidase inhibitors, and will allow for a cost-effective production method for lead candidates or products.
**Key Publications**


**Patent Position**

4. International PCT Application CA2010/000680, filed May 4, 2010

5. International PCT Application CA2009/001800, filed December 16, 2009


**The Market**

Our technology could be applicable to any mammalian Biologics production platform. Most cell lines used for manufacturing monoclonal antibodies and recombinant proteins (ie Biologics) are mammalian, including CHO, NS/O, BHK, 293 and murine hybridomas (ie hamster, mouse, human lines). In addition, we possess an unencumbered IP stance with regards to our compounds and the low-cost methods for their preparation. Considering glycosylated biotherapeutics comprise greater than 50% of an estimated $120 billion industry, there is significant market potential.

**Technology Transfer Possibilities**

- Development of this technology through a joint collaboration
- A commercial exploitation license for the technology

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