EP Vantage Interview - Prosensa’s antisense technology making sense to Glaxo

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As early stage collaborations go Prosensa is obviously doing something right. Today, the private Dutch biotechnology group announced that GlaxoSmithKline has agreed to develop a further three RNA modulating compounds in Duchenne muscular dystrophy (DMD) from its pipeline.

The deal, which extends an existing agreement, means that Prosensa is eligible to receive milestones and development funding payments of up to £27m ($43m). More importantly, it will leave the group in the very enviable position of having four products in the clinic next year, including one phase III drug, while providing non-dilutive funding, something that should please existing investors. Speaking to EP Vantage Luc Dochez, chief business officer at Prosensa, says the announcement is confirmation that the collaboration is going well. “Things are advancing and both parties see it as a strong partnership.”

Foundations

The original partnership was forged back in October 2009, when Glaxo licensed Prosensa’s PRO051, now known as GSK2402968, for an upfront fee of $25m and potential milestones of $655m. The deal saw Glaxo pay all development costs for ‘51 and also included the option to develop a further three DMD compounds.

The three new compounds now in the deal are Phase II candidate PRO044, and pre-clinical assets PRO045 and PRO053. As part of the deal Glaxo has an exclusive option to license ‘044 and either ‘045 or 053, leaving Prosensa with full development and commercialisation rights to the remaining compound. This time round Prosensa is also joining in with funding the development of the three new products.

Rare disease

DMD is caused by a mutation in the dystrophin gene, and mainly affects boys, who experience progressive muscle wasting and rarely live beyond 35 years.

The dystrophin gene is the largest in the body and consists of 79 exons. Exons are small sequences of genetic code that lead to the manufacture of proteins. In DMD when certain exons have mutations or are deleted RNA cannot read past the fault along the gene. This abrupt stop results in the production of non-functioning dystrophin protein and the symptoms of DMD.

Prosensa’s drugs are all antisense oligonucleotides and work by a process known as exon skipping. The oligonucleotides skip an exon next to a defective exon allowing the RNA to read past the fault, creating shorter, but still functioning dystrophin proteins.

Unmet medical need

GSK2402968, the most advanced product in the compound skips Exon 51, which accounts for 13% of DMD patients, and by licensing ‘044, ‘045 and ‘053 the collaboration will now cover approximately 35% of DMD patients - and there is more to come Mr Dochez says in order to try and treat as many patients as possible.

Prosensa has not said how many drugs it intends to develop but it has another two pre-clinical exon-skippers in the pipeline and the ability to generate more. There could therefore be further collaborations either with Glaxo or other pharma companies.

Antisense making sense

If successful, Prosensa’s treatments will one of the few disease-modifying products available for the rare disorder. It will also be an unusual example of a success in the antisense field, which has promised much and has yet to deliver.

“We’re hoping we can shift that trend and show that you can be very successful,” says Mr Dochez. “To date the data have been encouraging. Also in Duchenne the disease makes it very suitable for uptake for these kind of
molecules, so we hope we will be successful, if not for us but for all the patients that really deserve treatment.”

Analysts at least believe there is some chance of success. Although GSK2402968 is one of four phase III muscular dystrophy products, it is the only that has been assigned sales. Consensus forecasts from EvaluatePharma show a potential launch date of 2014 and sales of $147m by 2016.

Moving on

Having got Glaxo to take up its option the next steps for Prosensa are deciding how to spend some of its signing on fee. A portion of it will be spent on creating a natural history study with Glaxo on the progression of the disease depending on which of its therapies is used.

This says Mr Dochez is important because if the compounds work and subsequent treatments are developed it may not be possible or ethical to do placebo controlled trials making it essential to have a natural history study. He also believes that Glaxo’s involvement in this project is another sign of the pharma giant’s commitment to the development of a DMD franchise.

What might not be taking up so much of his time is thinking of funding, thanks to the Glaxo collaboration, which has already produced milestone payments.

Cash cushion

The collaboration has meant that the last time the group turned to its investors was in December 2008, when it raised $24m in a series B funding, taking its funding total to a relatively modest $42m.

But that said the group is not entirely ruling out finding additional financing. “We are a biotechnology company and by that definition we are always thinking about the next round of financing,” says Mr Dochez. “But we are also in a very healthy position, thanks to the strong collaboration and the good progress that has led to a number of funding milestones by GSK and they have taken over the cost of the phase III of the lead compound, which helps in conserving cash for a company.”

But Prosensa has ambitions of its own and is keen to develop its own products outside of the collaboration, so longer term it might look to fresh funding sources.

“The one [compound] they don’t take we will bring to the finishing line ourselves and we will commercialise this ourselves, so we will need more cash. So a financing is in our plans, but without us being with our backs to the wall and desperately needing it tomorrow,” Mr Dochez says.

Finding an exit

There are also grander plans to grow into a fully integrated, specialist rare disease company, a strategy that Mr Dochez says will realise the most value for its current investors.

But that vision will ultimately require the return of investor appetite for biotech flotations. He is, however, very aware that this might be a long-term exit strategy. “The IPO window is closed today, but maybe it won’t remain shut for the next 10 years,” he says.

As to a trade sale, despite the number of companies taking this route, its not Prosensa’s preferred option. “Yes a trade sale is never excluded, but it is not the primary goal of the company. We are all working hard to bring this forward and copy the success of independent companies such as BioMarin, Viropharma and the big success Genzyme.”

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