

# STORY OF A SPIN-OUT

**The AstraZeneca spin-out Albireo has carried on the global pharma's long tradition of drug development within the gastrointestinal area. Later this year, results from a phase IIb clinical trial with their lead program is expected.**

**T**HE BIG PHARMA AstraZeneca has had a long tradition of research within the gastrointestinal (GI) area. However, following a global strategy change the company decided to cut back on certain activities within this field and focus primarily on gastroesophageal reflux disease, including line extensions for the blockbuster Nexium. AstraZeneca had for a long time made large investments in preclinical research in the GI field and instead of terminating lower GI tract research completely, a new independent company financed by external investors was formed in 2008 on the AstraZeneca platform of GI projects.

“This had never been done within AstraZeneca before. GöteborgBIO was really supportive during the process of creating the spin-out. The financing came from a syndicate of growth capital firms, led by Nomura Phase4 Ventures,” says Jan Mattsson, Chief Operating Officer and co-founder of Albireo. The series-A equity financing resulted in \$40 million. AstraZeneca has significant minority equity interests but has no rights attached to the programs. Albireo owns all IP and product rights.



## Therapeutic area

Jan Mattsson and his colleagues at Albireo are developing novel therapeutic alternatives to fulfill medical needs primarily in the GI area. The lead program A3309, aimed for the indications chronic constipation and constipation predominant irritable bowel syndrome is currently in phase IIb. Chronic constipation is one of the most common digestive complaints with a prevalence of approximately 12-19% in North America and 8-26% in Europe. It is more common in women and the elderly. A3309 is aimed for the severe end of chronic constipation, e.g. for patients that do not respond to treatment with conventional over-the-counter therapies. The segment is estimated to be 2-4% of the total adult population and, due to the aging population and western lifestyle, the prevalence is also expected to increase. Since the symptoms overlap, many treatments that apply to chronic constipation patients also apply for patients with constipation-predominant irritable bowel syndrome (IBS-C). IBS causes pain in the abdomen and changes in the frequency of bowel movements and fecal consistency. It is most common among women of childbearing age and is the most common disorder diagnosed by gastroenterologists. The total constipation and IBS-C market today is worth \$3 billion. Business analysts estimate that the sale poten-



Biotech Centre, Gothenburg.



Jan Mattsson,  
Chief Operating Officer, Albireo.

tial for a new effective drug for constipation and IBS-C lies between \$600 million to \$1.6 billion.

## Novel mechanism

“A3309 is a first-in-class compound, with a novel physiological mechanism,” says Jan Mattsson. A3309 modulates the re-uptake of bile acids by inhibiting the Ileal Bile Acid Transporter (IBAT), also known as the Apical Sodium Dependent Bile Acid Transporter

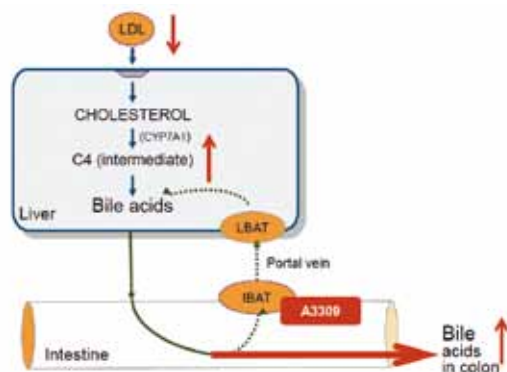
(ASBT). This results in an increased concentration of bile acids in the colon which, in turn, increase fluid secretion and colonic motility. A3309 is taken once daily. “These physiological responses should provide benefits to patients with chronic constipation and IBS-C,” says Jan Mattsson. “The drug acts locally in the gut and has minimal systemic exposure. Having a locally active drug is obviously a strong advantage and there are no similar treatments available today.”

## Clinical results

A Phase Ib/IIa study was completed by Albireo during last year showing a favorable tolerability and safety profile of A3309 in patients with chronic idiopathic constipation. In addition, the data revealed appropriate efficacy signals in this patient population. In the randomized, double-blind, placebo-controlled, prospective dose-escalating study, 30 patients were administered placebo or A3309 in a dose range of 0.1 mg – 10 mg for 14 days.

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In addition to evaluating safety and tolerability, bowel habits and gastrointestinal symptoms from patient diaries and radiographic assessments of transit were used to assess the efficacy of A3309. There were no serious adverse events reported and no patient discontinued the trial. Adverse events were evenly distributed across the different dose levels and no difference was observed compared to placebo. The mode of action – inhibition of bile acid re-absorption in the small bowel – was clearly demonstrated by biomarker analysis and colonic transit was improved in the higher dose groups as was the number of bowel movements. In addition, stool consistency improved. “The results certainly motivated us to move this compound further in development,” says Jan Mattsson.



**A3309 acts locally in the gut, modulating the re-uptake of bile acids by inhibiting the ileal bile acid transporter (IBAT).**

A3309 is currently being evaluated in a large phase IIb study in chronic constipation enrolling approximately 180 patients and further investigation of A3309's enhancement of large bowel transit is being conducted at the Mayo Clinic, USA. Also, given the mode of action, A3309 may be beneficial in patients with dyslipidemia and a study to evaluate A3309 in patients with high cholesterol levels is conducted in Sweden. Results of these clinical studies will be available late this year and plans are to move forward into Phase III in chronic constipation during 2011. “We are performing the phase IIb study in the US since it is one of the most important markets for this compound,” says Jan Mattsson. “A3309 is expected to be launched in 2014.”

Albireo also have additional IBAT inhibitors in the pipeline. One of the compounds, A4250, is in GLP toxicology phase and will

be ready for phase I studies by the end of the year.

## Preclinical programs

Albireo also has preclinical programs in the pipeline, primarily aimed for the treatment of Inflammatory Bowel Disease (IBD), e.g. ulcerative colitis and Crohn's disease. Existing therapies have either sub-optimal efficacy or safety and/or tolerability issues and there is still a great need for new and safe treatment options. The total IBD market is valued at approximately \$3 billion. “One of the programs aims to develop a neurokinin (NK) receptor antagonist as a treatment for IBD and/or IBS. It is potent for both NK1 and NK2 receptors and is efficacious in animal models. The program is in the late preclinical development phase,” says Jan Mattsson. Another program aims to develop a locally active peroxisome-proliferator activated receptor (PPAR) agonist as a treatment for IBD, as this mechanism of action has been clinically proven. It exhibits gastrointestinal anti-inflammatory effects and avoids systemic exposure. The program is currently at the stage of selecting candidates for safety and toxicology evaluations.

## Business strategy

Albireo today has eight employees, but in total, including collaborators and consultants, there are at certain times probably 40 persons involved in the development programs. “This is part of our strategy, outsourcing several parts of the business and working closely with expertise in areas that we do not cover internally,” says Jan Mattsson and explains more. “Our aim for the Series A financing is to develop A3309 to phase III-ready stage and also to extend the pipeline with one additional program in clinical phase. We want to develop multiple strategic options for the company during 2010 and 2011, where one important goal is to partner the A3309 program post phase IIb data.” He emphasizes the company's desire to in-license new innovative drug programs to add to the pipeline as an essential part of their strategy.

“We have a management team with extensive experience in drug development, in particular within the gastrointestinal area, covering all phases, from discovery to late development phase. We have now built a good

infrastructure for fast and effective drug development. In addition we have good contacts with investors in the biotech space,” he says.

## Strategically good location in Gothenburg

Albireo offices are located in the BioTech Center in Gothenburg, close to the Sahlgrenska University Hospital, Sahlgrenska Academy and Sahlgrenska Science Park. “Being located here is of course a strategically good location and if we need support we have it close by,” says Jan Mattsson. He likes the idea of gathering companies together and creating an atmosphere where collaborations can be more fruitful and small start-ups can grow. For the future of Albireo he has great expectations. “Short term, we want to continue to grow and strengthen our R&D pipeline with innovative drug programs. Longer term, we have a vision of a company with our own marketing & sale capacity for specialty GI indications and regional markets. Anyhow, the ultimate goal and the underlying driver for us is to develop drugs that will reach all the way to the patients, and make a difference in their lives.”

## GöteborgBIO

GöteborgBIO is a joint project between national and regional players. It aims to create a solid base for long-term growth in the biomedical field within the region, by cultivating academic research and commercial innovations and adaptations within the health care system.

GöteborgBIO has the following focus areas:

- Reinforcing the commercial turnover as a result of research and development within biomaterial and cell therapy.
- Educating and training future leaders in advanced business development within the biomedical field.
- Developing and reinforcing the infrastructure for the commercial development of projects within biomedicine.
- Attracting both expertise and capital to the biomedical field within the region.

Principals are AstraZeneca, Business Region Göteborg AB, Chalmers University of Technology, University of Gothenburg/The Sahlgrenska Academy, Innovationsbron AB, Mölnlycke Health Care AB, Nobel Biocare AB, VINNOVA and Region Västra Götaland.

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