January 2013

Global Life Science Ventures: 2012 Review

Dear Sir/ Madam,

as in previous years, let us share with you a retrospective look at major news and events in our portfolio over the last twelve months.

The biotech industry has weathered some storms worldwide since the financial crisis, but continues to come out with innovations and successes. In 2012, the FDA approved 40 novel drugs (15 being orphan drugs), an approval rate not seen in this industry since the 1990s. This comes as a relief as overall access to capital has become an increasing challenge for the entire industry worldwide. With diminishing venture capital, the funding model is changing, and more companies are pursuing grant funding, partnering with big pharma/biotech, corporate venture and angel investors than in the past. While biotech stocks fuelled by strong M&A activity have been a hot sector on Wall Street, with the Nasdaq Biotech Index having shot up 32% this year compared with 16% growth in the broader market, the level of IPOs did not exceed 2011. This stems from big pharma's preference for commercial-stage assets, rather than clinical trial-stage drugs carrying regulatory approval risk, which means that pharma tends to prefer multibillion-dollar transactions to smaller deals that do not offer immediate solutions to their threats resulting from one of the worst patent cliffs in history. However, the time when big pharma will again turn to innovative and earlier stage drugs, is difficult to foresee. Today, big pharma has ample of cash and easy access to cheap debt, allowing aggressive bids for promising biotech companies and other targets.

In this environment the portfolio companies of the combined GLSV II partnerships continue to focus on their most important development programs and on maintaining/extending their cash reach.

During 2012, GLSV II's portfolio decreased by four companies: **7TM** was exited through a management buy-out and **Fibrex** is in liquidation; in both cases, the proceeds returned to the investors, do not cover the acquisition cost. Furthermore, the remaining shares in the two public companies **NeurogesX** and **Zalicus** were sold. Major positive news in 2012 was the asset deal of **Action Pharma** with Abbott resulting in a payment of $110m, and the option deal by **Nabriva** with Forest Laboratories who paid $25m upfront for a call option to acquire the company within the next twelve months. Another important event was the deal between **Pixium**, a new company set up in Paris, and **IMI** whereby Pixium acquired all assets of IMI against shares. I.e., as per year end, the portfolio consists of one public company and six active private investments. All six of them raised capital in 2012 in form of debt and/or equity.

Apart from these financing rounds and exit events, the following news selection shows the ongoing progress made within GLSV II's portfolio:

In February, **Pieris** announced the receipt of a €1m grant to support the development of its proprietary PRS-110 compound targeting c-Met, a cellular receptor that plays a key role in cancer cell growth and metastasis. **Horizon** applied for extension of its DUEXIS® (ibuprofen/famotidine) marketing authorization to include the recently approved manufacturing site in Canada, which is used to manufacture DUEXIS for the United States market. Horizon also completed a $60m loan as well as a $50.8m equity financing. The proceeds will be used to repay $22.4m of venture loans, to fund the ongoing launch of DUEXIS® in the U.S., and to pursue regulatory approval for DUEXIS in Europe and LODOTRA® in the U.S.

In April, **Pieris** presented a range of *in vitro* and *in vivo* preclinical data for its c-Met antagonist program, PRS-110, at the annual meeting of the American Association for Cancer Research.

Santaris presented final data from a clinical Phase 2a trial showing that miravirsen given as a four-week monotherapy treatment provided robust dose-dependent anti-viral activity with a mean reduction of 2 to 3 logs from baseline in HCV RNA that was sustained well beyond the end of therapy. At the end of the month, **Santaris** announced that Søren Tulstrup, President and CEO, decided to leave the company per April 30, 2012, to pursue other opportunities. Henrik Stage, VP and CFO, will take over as interim CEO.

In May, **Action** sold all its global rights for AP214 to Abbott against a cash payment of $110m. AP214 is a phase IIb compound to prevent acute kidney injury associated with major cardiac surgery in patients at increased risk. **Agendia** raised $65m in a private equity round led by Debiopharm, a leading drug development company based in Switzerland, to fund the commercialization of its current breast cancer Symphony tests, as well as the ongoing development of its personalized medicine pipeline.

In June, **Agendia** announced the launch of its ColoPrint microarray-based 18-gene expression signature for predicting the risk of recurrence for stage II colon cancer patients who have undergone surgery. **Nabriva** Therapeutics and Forest Laboratories announced an agreement for the development of Nabriva's novel antibacterial agent, BC- 3781, whereby Forest will pay $25m to Nabriva, and fund and conduct in collaboration with Nabriva, certain development activities related to BC-3781 over the next 12 months. During this period, Forest has a call option to acquire Nabriva. **Santaris** completed a $12m round structured as convertible bonds, subscribed by existing investors and members of the management. The proceeds will be used primarily to fund development of its lead clinical phase II asset, Miravirsen, for the treatment of HCV infection, as well as of its world-leading LNA-platform.

In July, **Horizon** received the FDA approval for RAYOS® (prednisone) delayed-release tablets to treat a broad range of diseases including rheumatoid arthritis (RA), polymyalgia rheumatic (PR), psoriatic arthritis, ankylosing spondylitis, asthma and chronic obstructive pulmonary disease.

In August, **Agendia** received the ISO 13485 certification for all activities at their facilities in Irvine and Amsterdam. This certification confirms that Agendia's Symphony diagnostic services, including MammaPrint®, BluePrint™, TargetPrint® and TheraPrint®, meet the highest quality standards.

In September**, Santaris** announced that the federal court in the Southern District of California granted Santaris significant relief in the patent infringement lawsuit brought by Isis. **Horizon** raised another $81m in a public offering to fund its commercialization activities for DUEXIS® and RAYOS®.

In October, **Pieris** announced the achievement of the first financial milestone in its discovery and development collaboration with Daiichi Sankyo. The milestone recognizes the on-schedule selection, optimization and characterization of several Anticalin drug candidates, against a Daiichi Sankyo target.

In November, **Agendia** published the results of a study in the prestigious scientific Journal "Cell", identifying a gene signature associated with resistance to a broad range of cancer therapies in multiple cancer types. **Pieris** presented at the 8th Annual European Antibody Congress in Geneva, Switzerland, data for its PRS-190 bispecific Anticalin program targeting IL-17 and IL-23, two key members of the Th17 family of cytokines, involved in autoimmunity and hyperinflammation.

Finally, in December, **Horizon** announced that RAYOS® (prednisone) delayed release tablets (Nitec's former LODOTRA®) are now available for sale to U.S. physicians. The focus of the commercial launch by Horizon's sales force of approximately 150 representatives in January 2013 will be on RA and PR.

These developments are encouraging and give hope for further positive news after an extension of the life time of the fund in May 2013 as recommended by the General Partners and the Advisory Board. Terms are in discussions and a timely proposal will be submitted to all Limited Partners.

We thank you again for your support in the past and look forward to the continuation of our good relationship. Should you have any questions, please, do not hesitate to contact us at any time.

With kind regards,

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