Shire Adds to Rare Disease Portfolio with Acquisition of Lumena Pharmaceuticals, Bringing Late Stage Compounds for Rare GI/Hepatic Conditions

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Shire plc and Lumena Pharmaceuticals →
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DUBLIN and SAN DIEGO, May 12, 2014 /PRNewswire/ --

- Acquisition of Lumena Pharmaceuticals, a biopharmaceutical company with late stage rare disease pipeline assets
- Adds to Shire's rare diseases portfolio and leverages this expertise, and is a perfect combination with Shire's already strong Gastrointestinal (GI) presence
- Adds LUM001 in Phase 2 development for four rare and devastating hepatic diseases, two pediatric and two adult with a potential 2016 approval and LUM002 a Phase 2-ready candidate for the treatment of non-alcoholic steatohepatitis (NASH)
- Very attractive opportunity to develop treatments for significant unmet need in rare cholestatic liver diseases as well as a treatment for non-alcoholic steatohepatitis (NASH)
- Shire will acquire Lumena Pharmaceuticals for an upfront payment of $260 million in cash, plus a payment for net cash at closing, and near-term contingent milestone payments related to ongoing clinical trials
- These two compounds, and Shire's full portfolio, will be discussed in more detail at an Investor Day later in 2014.

Shire plc (LSE: SHP,NASDAQ: SHPG) and Lumena Pharmaceuticals, Inc., a biopharmaceutical company with rare disease pipeline assets, announce the acquisition of Lumena Pharmaceuticals by Shire.

Chief Executive of Shire, Flemming Ornskov, MD comments:

"Our pipeline and strategic focus on rare diseases is even further strengthened with the acquisition of Lumena Pharmaceuticals, which also complements our strong GI presence. These attractive potential treatments may offer new hope to patients with rare cholestatic liver disease and further contribute to Shire's future growth. We are excited by the possibilities of these new assets in liver disease. We have the resources, the infrastructure and the operating capacity to invest in these new potential growth drivers which add further value to Shire's innovative pipeline."

President and CEO of Lumena Pharmaceuticals, Mike Grey comments:

"I believe that this transaction is a significant win for all parties involved, especially the patients, and the future of LUM001 as a treatment for rare cholestatic liver diseases looks brighter than ever. Shire has deep rare disease experience, a global infrastructure, and the commercial expertise to deliver LUM001 to patients around the world. The Lumena team will work closely with Shire to finish the ongoing Phase 2 clinical programs as part of our commitment to the patient populations we have championed since we formed Lumena Pharmaceuticals."

Strategic rationale and background on Lumena Pharmaceuticals

The acquisition of Lumena strengthens Shire's already valuable and robust pipeline. It complements Shire's strategic focus on Rare Diseases and provides a future growth path for Shire's Gastrointestinal business, which generated revenues of over $800 million in 2013. In acquiring Lumena, Shire is gaining experience in liver disease with the opportunity to leverage its existing GI commercial infrastructure. In addition, there is a good fit with Shire's recent acquisition of Fibrotech, which has brought pipeline programs to address unmet patient need in other fibrotic conditions including renal impairment.

Lumena Pharmaceuticals brings to Shire two new oral therapeutic compounds; LUM001, in Phase 2 with four potential orphan indications and LUM002, ready to enter Phase 2 later in 2014.

LUM001 and LUM002 are both inhibitors of the apical sodium-dependent bile acid transporter (ASBT), which is primarily responsible for recycling bile acids from the intestine to the liver. Blocking bile acid transport with ASBT inhibitors reduces bile acid absorption and has the potential to improve liver function and relieve disease symptoms (such as extreme itching associated with cholestatic liver diseases), and may slow disease progression.

These rare cholestatic liver diseases are primarily treated by hepatologists and gastroenterologists and can be covered by a small, specialty sales force consistent with Shire's model.

Shire does not expect the acquisition of Lumena to result in a change to its previously stated earnings guidance for 2014.

About LUM001

LUM001 is a novel, once-daily, orally-administered, potent and selective ASBT inhibitor that works by preventing recycling of bile acids back to the liver and is thought to reduce bile acid accumulation, improve liver function and potentially relieve the extreme itching associated with cholestatic liver disease.

LUM001 is currently in Phase 2 clinical development for four rare cholestatic liver disease indications; two pediatric and two adult with a potential 2016 launch. These potential indications are: Alagille syndrome (ALGS), progressive familial intrahepatic cholestasis (PFIC), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC).

Some of the key characteristics of cholestatic liver diseases are elevated bile acids, leading to progressive liver damage that can cause liver failure, and pruritus, or severe itching. Pruritus is generally the most debilitating symptom afflicting children and adults with these diseases.

Surgical intervention, which lowers bile acid levels, has been shown to relieve symptoms and slow disease progression in patients with ALGS and PFIC - this is currently the only treatment option for these patients. Patients with cholestatic liver diseases may ultimately require liver transplants.

By reducing serum bile acids, LUM001 may offer a novel therapeutic approach for alleviating the pruritus and progressive liver damage associated with cholestatic liver diseases.

The prevalence of each of the four diseases is as follows:

Indication	US prevalence	EU prevalence
	3 per 100,000	
ALGS	9476 individuals	3 per 100,000
	<1 per 100,000	
PFIC	3159 individuals	1 per 100,000
	40 per 100,000	
PBC	126,979 individuals	30 per 100,000
	14 per 100,000	
PSC	44,222 individuals	3 per 100,000

(Source: Lumena Pharmaceuticals Applications for Orphan Designation):

LUM001 has received orphan drug designation for all four potential indications in both the United States and the European Union.

About LUM002

LUM002 is a novel, once daily, orally-administered, highly potent and selective inhibitor of ASBT, in development for the treatment of nonalcoholic steatohepatitis (NASH), a common and often "silent" liver disease characterized by fat deposits in the liver and inflammation which can progress to significant fibrosis.

While the underlying cause of liver injury in NASH is not fully known, it is strongly associated with obesity, Type 2 diabetes, high cholesterol and triglycerides, and other metabolic disorders. Approximately 6 million individuals in the US are estimated to have progressed to NASH and some 600,000 to NASH-related cirrhosis (Source: World Gastroenterology Organisation Global Guidelines June 2012).

By blocking bile acid reabsorption, LUM002 is thought to modulate colonic bile acid concentrations and receptor signaling on cells in the lower portion of the GI tract. This signaling is believed to result in the secretion of peptides that regulate insulin release from the pancreas, glucose metabolism and the synthesis of cholesterol and fatty acids.

Therapeutic strategies aimed at modulating insulin resistance and normalizing lipoprotein metabolism have significant potential to benefit patients with NASH.

Phase 1 safety trials in healthy volunteers and a Phase 1b trial in patients with metabolic disease have been completed. The next step is to initiate a Phase 2 clinical trial in patients with NASH - anticipated to begin in the second half of 2014.

NOTES TO EDITORS

About Lumena Pharmaceuticals

Lumena Pharmaceuticals is a privately held, San Diego-based, biopharmaceutical company founded in 2011 by Pappas Ventures. Other investors include Alta Partners, RiverVest Venture Partners, New Enterprise Associates, Adage Capital Management and RA Capital Management.

Citi acted as the exclusive financial advisor to Lumena.

About Shire plc

Shire enables people with life-altering conditions to lead better lives.

Our strategy is to focus on developing and marketing innovative specialty medicines to meet significant unmet patient needs.

We provide treatments in Neuroscience, Rare Diseases, Gastrointestinal and Internal Medicine and we are developing treatments for symptomatic conditions treated by specialist physicians in other targeted therapeutic areas.

http://www.shire.com

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Statements included in this announcement that are not historical facts are forward-looking statements. Forward-looking statements involve a number of risks and uncertainties and are subject to change at any time. In the event such risks or uncertainties materialize, Shire's results could be materially adversely affected. The risks and uncertainties include, but are not limited to, that:

- Shire's products may not be a commercial success;
- revenues from ADDERALL XR are subject to generic erosion and revenues from INTUNIV will become subject to generic competition starting in December 2014;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payors in a timely manner for Shire's products may impact future revenues, financial condition and results of operations;
- Shire conducts its own manufacturing operations for certain of its Rare Diseases products and is reliant on third party contractors to manufacture other products and to provide goods and services. Some of Shire's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of Shire's products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time.
- the development, approval and manufacturing of Shire's products is subject to extensive oversight by various regulatory agencies and regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the actions of certain customers could affect Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely impact Shire's revenues, financial conditions or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to Shire's activities in the highly regulated markets in which it operates may result in the distraction of senior management, significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including Shire's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on Shire's revenues, financial condition or results of operations;
- Shire faces intense competition for highly qualified personnel from other companies, academic institutions, government entities and other organizations. Shire is undergoing a corporate reorganization and the consequent uncertainty could adversely impact Shire's ability to attract and/or retain the highly skilled personnel needed for Shire to meet its strategic objectives;
- failure to achieve Shire's strategic objectives with respect to the acquisition of ViroPharma Incorporated may adversely affect Shire's financial condition and results of operations; and other risks and uncertainties detailed from time to time in Shire's filings with the U.S. Securities and Exchange Commission, including its most recent Annual Report on Form 10-K.

For further information please contact:
Shire
Investor Relations: Jeff Poulton, jpoulton@shire.com, +1-781-482 0945

Sarah Elton-Farr, seltonfarr@shire.com, +44-1256-894157

Media: Jessica Mann, jmann@shire.com, +44-1256-894-280

Gwen Fisher, gfisher@shire.com, +1-484-595-9836

Lumena Media contact: Heidi Chokeir, Ph.D., Canale Communications, Heidi@canalecomm.com, +1-619-203-5391

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