Seal Rock Therapeutics

Seal Rock Therapeutics Advancing Differentiated ASK1 Inhibitor Lead Candidate SRT-015 in NASH

Preclinical Findings Highlight Potent Efficacy in the Therapeutic DIO-NASH (Gubra) Mouse Model

International Patent Application for SRT-015 and Other ASK1 Inhibitors Published

November 9, 2018, Seattle, WA – Seal Rock Therapeutics, Inc., a discovery stage company developing best-in-class treatments for inflammatory and fibrotic diseases with no available therapies, today announced its lead compound, SRT-015, a differentiated inhibitor of apoptosis signal-regulating kinase 1 (ASK1) for nonalcoholic steatohepatitis (NASH), with promising preclinical proof-of-concept findings and recent worldwide patent application issued.

SRT-015 is a potent, liver-selective ASK1 inhibitor for NASH. The candidate was internally discovered and optimized by Seal Rock Therapeutics to improve upon and avoid dose-limiting liabilities demonstrated by other investigative approaches. Preclinical research of SRT-015 has demonstrated promising efficacy in the biopsy-proven, DIO-NASH Gubra therapeutic NASH mouse model. This includes statistically significant positive effects on both metabolic parameters and liver-specific pathology. In addition, SRT-015 significantly reduced hepatomegaly, liver fibrosis, steatosis and inflammation, all key drivers for NASH. These findings will be presented at the Keystone Symposia Integrated Pathways of Disease in NASH and NAFLD meeting, in Santa Fe, New Mexico, January 20–24, 2019.

“SRT-015 has a unique property that makes it particularly suitable for NASH: it is distributed to the liver where it is needed, but very little is present in the circulation or other tissues, which helps reduce risk of side effects and may allow for higher, more effective doses,” said Neil McDonnell, Chief Executive Officer of Seal Rock Therapeutics. “Our preclinical findings are proving very robust, and we are pleased to be advancing with IND-enabling activities for SRT-015.”

Additionally, Seal Rock Therapeutics announced the publication of an international PCT patent application for SRT-015 that includes ASK1 inhibitor compounds and uses thereof. The Patent Cooperation Treaty (PCT) is an international patent law treaty that includes 151 countries and covers all major pharmaceutical markets worldwide.

Seal Rock Therapeutics’ founders include Neil McDonnell, PharmD; Artur Plonowski, MD, PhD, Chief Scientific Officer; and; Kathleen Elias, PhD, Vice President Research & Translational Medicine.

Dr. McDonnell previously served as CEO of Metacrine and senior vice president and therapeutic area leader for cardiovascular and metabolic diseases at Takeda. He has been involved in the development of diabetes drugs Nesina (alogliptin), Oseni (alogliptin

+ pioglitazone), and Kazano (alogliptin + metformin), and with Takeda's partner Orexigen, the obesity drug Contrave (bupropion and naltrexone).

Dr. Plonowski recently served as director of pharmacology at Akarna Therapeutics, Ltd, a NASH start-up that was acquired by Allergan in 2016 for $50 million and $1 billion in milestones. Prior to Akarna, he led the cardiovascular, renal and metabolic disease pharmacology group at Takeda Pharmaceuticals, and served for 10 years at Exelixis with scientific and leadership responsibilities in CV, metabolic, renal, oncology, and inflammation therapeutic areas.

Dr. Elias previously served as director of preclinical research at Takeda, and led efforts to develop small molecule, antibody and antibody drug conjugates for immune, metabolic and oncology indications. Prior to that, at Cytokinetics, she established and led the cell biology and pharmacology efforts to identity and develop a myosin activator therapeutic for heart failure, and at Genentech, identified therapeutics for endocrine and cardiac indications.

Additional members of the Seal Rock leadership team include Terry Porter, PhD, Senior Vice President, Business Development; and David Brown, PhD, Director, Chemistry.

Dr. Porter previously served as vice president of search & evaluation within global business development at Takeda Pharmaceuticals. Prior to that, he was managing director at the corporate advisory group AquaPartners. He was also a senior member of the worldwide business development group at GlaxoSmithKline. During this time, he headed oncology licensing, created and led the external science and technology group and co-led GSK's $450 million acquisition of Domantis.

Dr. Brown recently directed the medicinal chemistry team at Pathway Therapeutics, which led to the selective PI3Kdelta kinase inhibitor PWT143/MEI-401. Prior to that, he spent 12 years at Exelixis where his kinase work contributed to 5 clinical candidates in the areas of oncology and inflammation.

About NASH NASH is a form of non-alcoholic fatty liver disease (NAFLD) that affects one in four individuals worldwide, making it one of the most common chronic liver diseases. NAFLD is associated with metabolic conditions such as obesity, diabetes, and high cholesterol. NAFLD is typically characterized as either fatty liver or steatohepatitis. Fatty liver is generally non-progressive or progresses slowly compared to steatohepatitis. NASH, which is steatohepatitis not caused by alcohol, is characterized by inflammation of the liver, which progresses to fibrotic remodeling (scarring) in 30-50% of individuals, increasing the risk for cirrhosis, liver decompensation, and hepatocellular carcinoma (HCC, liver cancer). NASH is currently the second leading cause of liver transplantation overall, and the leading cause in women. Pharmacologic therapy is not yet available, but NASH is increasingly a focus of drug development efforts.

About Seal Rock Therapeutics Seal Rock Therapeutics is a privately held, discovery stage company based in Seattle focused on the development of best-in-class treatments for inflammatory and fibrotic diseases with no available therapies. The company's lead product candidate, SRT-015, is a differentiated ASK1 inhibitor for NASH. Seal Rock is led by an experienced management team with a track record of successful drug discovery, development and commercialization. For more information, please visit www.sealrocktx.com
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November 2, 2020, Seattle, WA – Seal Rock Therapeutics, Inc., a preclinical stage company developing first-in-class and best-in-class treatments for severe liver diseases with limited or no available therapies, today announced two upcoming poster presentations showing data on the company's lead clinical candidate, SRT-015, a well-differentiated, liver-selective apoptosis signal-regulating kinase (ASK1) inhibitor for treatment of non-alcoholic steatohepatitis (NASH) and other liver diseases, at The Liver Meeting® 2020, the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD), which is taking place virtually November 13-16, 2020. These presentations will show comparative preclinical efficacy and pharmacokinetic findings on SRT-015.

"Our presence at The Liver Meeting reflects the promising data we have compiled on SRT-015. These posters will show excellent efficacy of SRT-015 in NASH-relevant models, and comparator data with the ASK1 inhibitor selonsertib that is consistent with its lack of efficacy in phase 3 trials. Our data provide potential explanations for these failures and suggest that ASK1 inhibition remains an important therapeutic strategy for inflammatory and fibrotic diseases," said Neil McDonnell, Chief Executive Officer of Seal Rock Therapeutics. "This highlights the potential of SRT-015 to be a first-in-class ASK1 inhibitor for patients with NASH and other indications, prompting us to prepare for clinical trials, which we expect will begin in early 2021."

Presentation details are as follows:

Abstract #1692:

Reduction of Hepatocyte Injury by SRT-015, a Novel Inhibitor of Apoptosis Signal-Regulating Kinase 1 (ASK1)

Artur Plonowski, Kathleen Elias, S. David Brown, Sanne Veidal, Kristoffer Rigbolt, Michael Feigh, Terence Porter, Neil D. McDonnell

Session: NAFLD and NASH Therapeutics – Pharmacologic and Other

Date/Time: Friday, Nov. 13, 2020 6 a.m. to 11:55 p.m.

Abstract #1658:

Anti-fibrotic and Anti-Inflammatory Mechanisms of Best-in-Class ASK1 Inhibitor SRT-015

Kathleen Elias, Artur Plonowski, S. David Brown, Sanne Veidal , Kristoffer Rigbolt, Michael Feigh, Neil D. McDonnell

Session: NAFLD and NASH Therapeutics – Pharmacologic and Other

Date/Time: Friday, Nov. 13, 2020 6 a.m. to 11:55 p.m.

About NASH

NASH (non-alcoholic steatohepatitis) is a severe, life-threatening condition resulting from fatty liver disease, characterized by hepatic inflammation and cellular damage that lead to liver fibrosis.

About Seal Rock Therapeutics

Seal Rock Therapeutics is a privately held, preclinical stage company based in Seattle focused on developing ~~a~~ first-in or best-in-class treatments for severe liver diseases with limited or ~~(~~no available therapies. Seal Rock is led by an experienced management team with a track record of successful drug discovery, development and commercialization. The company's lead product candidate, SRT-015, is a liver-selective, first-in-class ASK1 inhibitor for NASH and other severe liver diseases and is anticipated to enter into clinical trials in early 2021. For more information, please visit www.sealrocktx.com

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