Alnylam Pharmaceuticals and Ironwood Pharmaceuticals Enter U.S. GI Disease Education and Promotional Agreement for Alnylam's Givosiran in Acute Hepatic Porphyria (AHP)

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– Patients living with AHP suffer from chronic debilitating symptoms such as severe abdominal pain and often seek care from gastroenterologists –

– Alnylam to leverage Ironwood's leading capabilities in GI to help raise AHP awareness and bring givosiran (if approved) to gastroenterologists and other healthcare practitioners in the U.S. –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 13, 2019-- Alnylam Pharmaceuticals, Inc. (NASDAQ: ALNY), the leading RNAi therapeutics company and Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD), a GI healthcare company, announced today a U.S. GI disease education and promotional agreement for Alnylam's givosiran, an investigational RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) for the potential treatment of AHP. Givosiran has received Priority Review designation and Breakthrough Therapy Designation from the U.S. FDA, as well as Orphan Drug Designation in the U.S. The Prescription Drug User Fee Act (PDUFA) date for givosiran is set for February 4, 2020.

Under the terms of the agreement, Ironwood will provide AHP disease education to gastroenterologists and other healthcare practitioners that Ironwood currently calls on for LINZESS® (linaclotide). If approved by the U.S. FDA, Ironwood clinical sales specialists will then begin givosiran promotional efforts, augmenting Alnylam's broader commercialization activities.

"AHP is a rare disease with chronic, debilitating, and sometimes life-threatening attacks. Nearly all patients living with AHP consult at least one, if not several, gastroenterologists due to the recurring abdominal pain associated with their disease and are often misdiagnosed due to minimal disease awareness and a limited number of treatment options," said Barry Greene, President of Alnylam. "As Alnylam prepares for the potential launch and commercialization of givosiran around the world, leveraging Ironwood's U.S. GI commercial expertise and depth of relationships within the GI community represents a significant opportunity to expand medical education and diagnosis for patients with AHP."

"We are excited about the opportunity to partner with Alnylam to increase awareness among healthcare providers about the devastating effects of AHP and, if approved, to then discuss givosiran as a potential new treatment option for patients suffering from this severe, potentially life-threatening disease," said Tom McCourt, President of Ironwood.

The non-exclusive agreement covers an approximately three-year term. Ironwood will collaborate with Alnylam on AHP disease education designed to help ensure AHP patients are accurately diagnosed and to support access to treatment with givosiran once prescribed (assuming approval). Ironwood will receive fixed payments and royalties in the mid-teens percent on net sales generated from prescriptions or referrals from certain physicians related to Ironwood's promotional efforts. Alnylam will maintain responsibility for all other aspects of givosiran, and retains all global development and commercialization rights.

About Acute Hepatic Porphyria
Acute hepatic porphyria (AHP) refers to a family of rare, genetic diseases characterized by potentially life-threatening attacks and for some patients chronic debilitating symptoms that negatively impact daily functioning and quality of life. AHP is comprised of four subtypes, each resulting from a genetic defect leading to deficiency in one of the enzymes of the heme biosynthesis pathway in the liver: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and ALAD-deficiency porphyria (ADP). These defects cause the accumulation of neurotoxic heme intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), with ALA believed to be the primary neurotoxic intermediate responsible for causing both attacks and ongoing symptoms between attacks. Common symptoms of AHP include severe, diffuse abdominal pain, weakness, nausea, and fatigue. The nonspecific nature of AHP signs and symptoms can often lead to misdiagnoses of other more common conditions such as irritable bowel syndrome, appendicitis, fibromyalgia, and endometriosis, and consequently, patients afflicted by AHP often remain without a proper diagnosis for up to 15 years. In addition, long-term complications of AHP and its treatment can include chronic neuropathic pain, hypertension, chronic kidney disease and liver disease, including iron overload, fibrosis, cirrhosis and hepatocellular carcinoma. Currently, there are no treatments approved to prevent debilitating attacks or to treat the chronic manifestations of the disease.

About Givosiran
Givosiran is an investigational, subcutaneously administered RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) in development for the treatment of acute hepatic porphyria (AHP). Monthly administration of givosiran has the potential to significantly lower induced liver ALAS1 levels in a sustained manner and thereby decrease neurotoxic heme intermediates, aminolevulinic acid (ALA) and porphobilinogen (PBG), towards normal levels. By reducing accumulation of these intermediates, givosiran has the potential to prevent or reduce the occurrence of severe and life-threatening attacks, control chronic symptoms, and decrease the burden of the disease. Givosiran utilizes Alnylam's Enhanced Stabilization Chemistry ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index. The safety and efficacy of givosiran were evaluated in the ENVISION Phase 3 trial with positive results; these results have not been evaluated by the FDA, the EMA or any other health authority.

About Alnylam Pharmaceuticals
Alnylam (Nasdaq: ALNY) is leading the translation of RNA interference (RNAi) into a whole new class of innovative medicines with the potential to transform the lives of people afflicted with rare genetic, cardio-metabolic, hepatic infectious, and central nervous system (CNS)/ocular diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of severe and debilitating diseases. Founded in 2002, Alnylam is delivering on a bold vision to turn scientific possibility into reality, with a robust discovery platform. Alnylam's first commercial RNAi therapeutic is ONPATTRO ® (patisiran), approved in the U.S., EU, Canada, and Japan. Alnylam has a deep pipeline of investigational medicines, including five product candidates that are in late-stage development. Looking forward, Alnylam will continue to execute on its "Alnylam 2020" strategy of building a multi-product, commercial-stage biopharmaceutical company with a sustainable pipeline of

RNAi-based medicines to address the needs of patients who have limited or inadequate treatment options. Alnylam employs over 1,200 people worldwide and is headquartered in Cambridge, MA. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam or on LinkedIn.

About Ironwood Pharmaceuticals
Ironwood Pharmaceuticals (Nasdaq: IRWD) is a GI-focused healthcare company dedicated to creating medicines that make a difference for patients living with GI diseases. We discovered, developed and are commercializing linaclotide, the U.S. branded prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC).

We are also advancing two late-stage, first-in-category GI product candidates: IW-3718 is a gastric retentive formulation of a bile acid sequestrant being developed for the potential treatment of persistent gastroesophageal reflux disease, and MD-7246 is a delayed-release formulation of linaclotide that is being evaluated as an oral, intestinal, non-opioid, pain-relieving agent for patients suffering from abdominal pain associated with IBS with diarrhea.

Ironwood was founded in 1998 and is headquartered in Cambridge, Mass. For more information, please visit our website at www.ironwoodpharma.com or www.twitter.com/ironwoodpharma; information that may be important to investors will be routinely posted in both these locations.

Alnylam Forward Looking Statements
Various statements in this release concerning Alnylam's future expectations, plans and prospects, including, without limitation, Alnylam's views with respect to the potential benefits of givosiran, the expected timing of the completion of regulatory reviews of the NDA submitted for givosiran, the anticipated benefits of the agreement entered into with Ironwood and the potential payments to Ironwood under such agreement, and expectations regarding its “Alnylam 2020” guidance for the advancement and commercialization of RNAi therapeutics, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other factors, including, without limitation, Alnylam's ability to discover and develop novel drug candidates and delivery approaches, successfully demonstrate the efficacy and safety of its product candidates, the pre-clinical and clinical results for its product candidates, which may not be replicated or continue to occur in other subjects or in additional studies or otherwise support further development of product candidates for a specified indication or at all, actions or advice of regulatory agencies, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing, delays, interruptions or failures in the manufacture and supply of its product candidates, obtaining, maintaining and protecting intellectual property, Alnylam's ability to enforce its intellectual property rights against third parties and defend its patent portfolio against challenges from third parties, obtaining and maintaining regulatory approval, pricing and reimbursement for products, progress in continuing to establish a commercial and ex-United States infrastructure, successfully launching, marketing and selling its approved products globally, Alnylam’s ability to successfully expand the indication for ONPATTRO in the future, competition from others using technology similar to Alnylam's and others developing products for similar uses, Alnylam's ability to manage its growth and operating expenses, obtain additional funding to support its business activities, and establish and maintain strategic business alliances and new business initiatives, Alnylam's dependence on third parties for development, manufacture and distribution of products, the outcome of litigation, the risk of government investigations, and unexpected expenditures, as well as those risks more fully discussed in the “Risk Factors” filed with Alnylam's most recent Annual Quarterly Report on Form 10-QK filed with the Securities and Exchange Commission (SEC) and in other filings that Alnylam makes with the SEC. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam explicitly disclaims any obligation, except to the extent required by law, to update any forward-looking statements.

Ironwood Forward Looking Statements
This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements including statements about the anticipated benefits of the disease education and promotional agreement entered into with Alnylam, the potential payments to Ironwood under such agreement, the effect of Ironwood’s disease education activities and promotional efforts (if approved) on Alnylam’s givosiran, and the development, launch, commercial availability and commercial potential of linaclotide and Ironwood’s other product candidates. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include, but are not limited to, the risk that Ironwood does not realize the benefits of the disease education and promotional agreement entered into with Alnylam, the effectiveness of Ironwood’s development and commercialization efforts, the risk that Ironwood’s clinical programs and studies may not progress or develop as anticipated, including that studies are delayed or discontinued for any reason such as safety, tolerability, enrollment, manufacturing, economic or other reasons, the risks that findings from Ironwood’s completed studies may not be replicated in later studies, the efficacy, safety and tolerability of linaclotide and Ironwood’s other product candidates and the risks listed under the heading “Risk Factors” and elsewhere in Ironwood’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, and in Ironwood’s subsequent SEC filings. These forward-looking statements speak only as of the date of this press release, and Ironwood undertakes no obligation to update these forward-looking statements.

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