RareStone Group & Rhythm Pharmaceuticals Announce Exclusive Licensing Agreement for the Development and Commercialization of IMCIVREE (setmelanotide) in China

-- RareStone to seek marketing authorization for IMCIVREE to treat obesity due to biallelic POMC, PCSK1 and LEPR deficiencies and Bardet-Biedl and Alström syndromes in mainland China, Hong Kong and Macau –

BOSTON, December 2, 2021 -- RareStone Group, a rare disease focused company aiming to establish the first rare disease ecosystem in China, Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a biopharmaceutical company aimed at developing and commercializing therapies for the treatment of rare genetic diseases of obesity, today announced an exclusive licensing agreement for the development and commercialization of IMCIVREE® (setmelanotide) in Greater China, including mainland China, Hong Kong and Macau. This licensing agreement is designed to accelerate patient access to IMCIVREE where there remains significant unmet need to address the severe, early-onset obesity and hyperphagia that characterize genetic and acquired diseases of the POMC-melanocortin pathway.

According to the terms of the agreement, RareStone will seek local approvals to commercialize IMCIVREE for the treatment of obesity and hyperphagia due to biallelic proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency, as well as Bardet-Biedl and Alström syndromes. Additionally, RareStone will fund efforts to identify and enroll patients from Greater China in Rhythm' s global EMANATE trial, a Phase 3, randomized, double-blind, placebo-controlled trial (with five independent sub-studies) to evaluate setmelanotide in patients with obesity due to a heterozygous variant of POMC/PCSK1 or LEPR; certain variants of the SRC1 gene, certain variants of the SH2B1 gene, or PCSK1 N221D deletions within the MC4R pathway.

"There is a significant need in China for a therapeutic option to treat patients with early-onset, severe obesity and hyperphagia caused by variants in genes of the POMC-melanocortin pathway," said Shawn Xiang, Ph.D., CEO of RareStone. "A recent, non-interventional genotyping study in China showed that 2.6% of 4,000 patients with obesity had a genetic variant with known relevance to obesity, and we look forward to building on that study with several key providers of genetic testing in China. In addition, we are eager to deliver the proven clinical benefit of IMCIVREE to patients in China and plan to pursue local approvals rapidly in five initial indications, while supporting Rhythm' s ongoing clinical development efforts more broadly."

"RareStone, a company committed to treating rare diseases, is well-

positioned to leverage its network of hospitals and key opinion leaders, deep regulatory experience and community-building infrastructure to advance IMCIVREE through clinical development and regulatory approvals in Greater China," said David Meeker, M.D., Chair, Chief Executive Officer and President of Rhythm. "We are thrilled to enter into this agreement, which substantially accelerates our ability to address the needs of patients living in Greater China and potentially make IMCIVREE available to many more patients with rare genetic diseases of obesity."

About RareStone Group

RareStone Group is dedicated to building the first rare disease ecosystem in China to improve the lives of patients and families impacted by rare diseases with comprehensive and sustainable solutions. RareStone Group consists of two business subsidiaries: Citrine Medicine and Zircon Health. RareStone Group was founded by Eight Roads Ventures, F-Prime Capital, and Vivo Capital in 2019 and closed a USD 80 million Series A financing in July 2020.

Citrine Medicine is a pharmaceutical company aiming to provide effective and affordable treatment solutions to rare disease patients in China. Citrine Medicine is building a comprehensive rare disease product platform through fast licensing and co-development to support and accelerate scalable commercialization. Citrine Medicine currently focuses on four therapeutic areas: neuroscience, endocrine & metabolic

diseases, liver & kidney diseases, and rare pediatric oncology. Citrine currently has six assets in the pipeline. Among these, three assets are licensed from global partners and are now in the pre-NDA stage in China (WAKIX® indicated for narcolepsy, Alkindi® indicated for pediatric CAH, and Efmody® indicated for adult CAH); another three assets are in-house developed assets targeting LSD related diseases and are currently in IND-enabling stage in China.

Zircon Health is a Health technology company aiming to build the largest patient-centered open ecological service platform in China with the help of cutting-edge technology. Zircon Health will leverage Internet digital tools, big data, and artificial intelligence technologies to improve the awareness of rare diseases, promote disease screening and diagnosis, carry out full-cycle disease management, and explore various payment innovations, providing comprehensive and one-stop health service solutions for patients and families affected by rare diseases. Zircon Health will focus on directly engaging and empowering patients and patient organizations to help the rare disease community in China improve access to knowledge, access to care, access to payment, and access to non-treatment solutions.

For more information, visit www.rarestonegroup.com

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About Rhythm Pharmaceuticals

Rhythm is a commercial-stage biopharmaceutical company committed to transforming the treatment paradigm for people living with rare genetic diseases of obesity. Rhythm' s precision medicine, IMCIVREE (setmelanotide), was approved in November 2020 by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency confirmed by genetic testing and in July and September 2021, respectively, by the European Commission (EC) and Great Britain' s Medicines & Healthcare Products Regulatory Agency (MHRA) for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. IMCIVREE is the first-ever FDA-approved and EC- and MHRA-authorized therapy for patients with these rare genetic diseases of obesity. The Company submitted a supplemental New Drug Application (sNDA) to the FDA, which was accepted for filing in September November 2021 and assigned a Prescription Drug User Fee Act (PDUFA) goal date of March 16, 2022. Rhythm also submitted a Type II variation application to the European Medicines Agency in October 2021 seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS or Alström syndrome in the European Union. Additionally, Rhythm, along with its partners, is advancing a broad clinical development program for setmelanotide in other rare genetic diseases of obesity and

is leveraging the Rhythm Engine, the largest known obesity DNA database -- now with approximately 45,000 sequencing samples -- to improve the understanding, diagnosis and care of people living with severe obesity due to certain genetic deficiencies. Rhythm's headquarters is in Boston, MA.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy, and regulatory and clinical progress of setmelanotide, including the anticipated timing for initiation of clinical trials and release of clinical trial data and our expectations surrounding potential regulatory submissions, approvals and timing thereof, our business strategy and plans, including regarding commercialization of setmelanotide, our participation in upcoming events and presentations, and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations. Statements using word such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, the impact of our management transition, our ability to enroll patients in clinical trials, the

design and outcome of clinical trials, the impact of competition, the ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, our liquidity and expenses, the impact of the COVID-19 pandemic on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and general economic conditions, and the other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 and our other filings with the Securities and Exchange Commission. Except as required by law, we undertake no obligations to make any revisions to the forward-looking statements contained in this release or to update them to reflect events or circumstances occurring after the date of this release, whether as a result of new information, future developments or otherwise.

琅钰集团与 Rhythm 签订 Imcivree 中国开发和商业化独家许可协议

中国上海和美国波士顿，2021 年 12 月 6 日 – 琅钰集团和 Rhythm Pharmaceuticals, Inc. （纳斯达克：RYTM）于今日宣布已达成独家许可协议，双方将携手在中国市场开发和商业化用于治疗一系列罕见遗传性肥胖疾病的治疗药物 IMCIVREE™(setmelanotide)。

IMCIVREE™(setmelanotide) 是由 Rhythm Pharmaceuticals 研发的黑素细胞皮质激素 4 受体 (*melanocortin 4 receptor, MC4R*) 激动剂。IMCIVREE™(setmelanotide) 作为一种精准靶向药物，能够恢复受损 MC4R 通路的功能，重新修复罕见病遗传性肥胖患者在能量消耗和食欲控制上的功能，减少饥饿感并降低体重。阿黑皮素原 (*Proopiomelanocortin, POMC*)、前蛋白转化酶枯草溶菌素 1 (*proprotein convertase subtilisin/kexin type 1, PCSK1*) 或瘦素受体 (*leptin receptor, LEPR*) 双等位基因缺陷可导致早发的严重肥胖，患者从很小的时候就不得不与极端饥饿作斗争。IMCIVREE™目前已在美国和欧洲上市，是全球首个获批的，用于治疗这一类罕见遗传性肥胖疾病的药物疗法。

根据协议条款，琅钰将优先就部分适应症寻求在中国的监管批准和商业化，包括：由 *POMC* 双等位基因缺陷、*PCSK1* 双等位基因缺陷、*LEPR* 双等位基因缺陷、 Bardet-Biedl 综合征或 Alström 综合征导致的罕见病肥胖和暴食。此外，琅钰还将积极推进 IMCIVREE 在全球的临床开发，包括但不限于招募中国患者入组全球 EMANATE 试验。

琅钰集团首席执行官向宇博士表示：“中国患者迫切需要一种治疗方案，来治疗由阿片黑素促皮质激素原 -黑素皮质蛋白通路基因变异引起的罕见遗传性肥胖患者。Rhythm 公司的精准治疗药物 IMCIVREE (setmelanotide) 已获得 FDA 和世界其他主要权威机构的批准，改变了罕见遗传性肥胖疾病的治疗模式。我们迫切地希望 IMCIVREE 能尽快惠及中国患者，解决中国患者的巨大治

疗需求。琅钰集团在中国市场已建立罕见内分泌/代谢疾病业务，并拥有丰富的临床开发、注册和商业化推进能力，此次合作将结合 Rhythm 在罕见遗传性肥胖疾病方面的专长，以及琅钰集团在中国市场的丰富经验，加速 IMCIVREE™在中国和全球市场的开发和商业化。**我们已着手推动 5 个罕见遗传性肥胖适应症在中国的临床开发，同时还将支持在全球范围内针对 IMCIVREE 开展的更为广泛的临床开发工作。**”

“中国市场对 Rhythm 具有战略意义。琅钰集团是一家致力于罕见病研发和商业化的公司，能够充分利用其在中国市场丰富的商业化经验和与患者社群的紧密连接，加速推动 IMCIVREE 在中国的临床开发和商业化上市。” **Rhythm 董事长、首席执行官兼总裁、医学博士 David Meeker** 表示，“我们很高兴能签署这项协议，这大大加快了我们触达中国患者的能力，让更多患有罕见遗传性肥胖疾病的患者能用上 IMCIVREE。”

部分接受 IMCIVREE™（setmelanotide）治疗的 POMC 缺陷肥胖症患者（Rhythm 提供）

“我们将用琅钰速度，尽早让中国罕见遗传性肥胖患者获益”

根据许可协议，琅钰集团将向 Rythmn 以现金和股票形式支付预付款以及与开发和商业化相关的里程碑付款，并基于中国市场年销售净额向 Rythmn 支付销售分成。

关于琅钰集团

琅钰集团致力于成为中国最领先的罕见病企业，通过打造中国首个罕见病生态系统，为受罕见病影响的患者和家庭提供全方位且可持续的支持。琅钰集团由全球领先的医疗基金斯道资本、F-Prime 资本和维梧资本共同创办，并于 2020 年 7 月完成 8000 万美元的 A 轮融资。

琅钰集团旗下目前有两家子公司：专注罕见病药物研发和商业化的“琅铌医药”和为广大罕见病患者和家庭提供医疗解决方案的“子昂健康”。琅铌医药是一家专注于罕见病药物研发和商业化的公司，致力于通过研发和引进有效且可负担的药物，建立一个综合的罕见病产品平台，以支持和加速可扩展的商业化进程。琅铌医药现阶段专注四大疾病领域：神经科学、内分泌系统和代谢类疾病、肝肾疾病、和儿童肿瘤。子昂健康是一家健康科技公司，致力于借助尖端科技打造中国乃至全世界最大的以患者为中心的开放式生态服务平台。子昂健康利用互联网数字化工具、大数据和人工智能技术，来提高罕见病认知、促进疾病筛查和诊断、开展全周期的疾病管理，并探索各种支付创新，为中国罕见病患者及家庭提供全病程、全方位和一站式的健康服务解决方案。子昂健康目前业务范围包括：罕见病智库、 AI 赋能的患者识别、AI 空中课堂、在线健康咨询、患者赋能及创新支付等。
琅钰集团总部位于中国上海，在香港、北京和马萨诸塞州剑桥也有办事处。欲了解更多信息，请访问 www.rarestonegroup.com

关于 Rhythm Pharmaceuticals

Rhythm Pharmaceuticals 是一家处于商业化阶段的生物制药公司，致力于改变罕见肥胖遗传疾病患者的治疗模式。Rhythm 的精准治疗药物 IMCIVREE™ （setmelanotide）于 2020 年 11 月获美国食品和药物管理局（FDA）批准，用于 *POMC*、*PCSK1* 或 *LEPR* 缺陷导致罕见遗传性肥胖的成人和 6 岁以上儿童患者的长期体重管理，并分别于 2021 年 7 月和 9 月，获欧洲委员会（EC）和英国药物和保健产品监管署（MHRA）批准，治疗特定基因突变所致功能丧失引起的罕见遗传性肥胖和暴食，包括确认为 *POMC* 缺陷、*PCSK1* 缺陷或 *LEPR* 缺陷的成人和 6 岁及以上儿童患者。

IMCIVREE™是第一个在全球范围内获得批准的治疗这些罕见遗传性肥胖疾病的药物疗法。该公司分别于 2021 年 9 月和 10 月提交了 FDA 补充新药申请（sNDA）和欧洲药品管理局（European Medicines Agency）第二类变更申请，寻求监管部门批准和授权 IMCIVREE™用于 Bardet-Biedl 综合征或 Alström 综合征的成人和 6 岁及以上儿童的肥胖管理和食欲控制。
Rhythm 的总部位于马萨诸塞州波士顿 。