Eluminex Biosciences Acquires Zuretinol Acetate from Retinagenix Holdings

- Purchase of Assets and Related Global Commercialization Rights for Oral 9-*cis*-Retinol (Zuretinol) for Rare Forms of Childhood Blindness.
- Clinical Stage Asset Has Potential for First Approved Oral Therapy for Leber's Congenital Amaurosis (LCA) and Retinitis Pigmentosa (RP) Caused by Mutations of the RPE65 or Lecithin:Retinol Acyltransferase (LRAT)
- Program Has Received FDA Rare Pediatric Disease and Fast Track Designation and is Eligible for a Rare Pediatric Disease Priority Review Voucher.
- Future Applications of Zuretinol Include Treatment of Impaired Dark Adaptation (Night Blindness) in Adult Patients with Early Dry Age-related Macular Degeneration (AMD).

SUZHOU, China and SAN FRANCISCO, January 19, 2022 (PR Newswire) – Eluminex Biosciences (Suzhou) Limited (Eluminex), an ophthalmology-focused biotechnology company headquartered in Suzhou, China with a US-subsidiary office in the San Francisco Bay Area, California, announced today that it has acquired certain assets and the related global development and commercialization rights for a novel oral therapy, zuretinol acetate (zuretinol), from Retinagenix Holdings, LLC (Retinagenix), a privately-held ophthalmic company based in Seattle, Washington. Zuretinol is an investigational treatment that is currently being developed to treat rare forms of childhood blindness in patients with LCA or RP caused by mutations of the RPE65 or LRAT gene.

"The addition of zuretinol into our growing retinal disease pipeline further bolsters our commitment towards the development of innovative therapies for vision-threatening diseases around the world," said Charles Semba, MD, Chief Medical Officer of Eluminex. "Currently, the only approved treatment for LCA and RP due to RPE65 and LRAT mutations is gene therapy which requires the child to undergo surgery and can treat only a small portion of the retina. Zuretinol offers hope in the ability to treat the entire retina and both eyes simultaneously either as a monotherapy treatment or adjunctive to gene therapy in restoring vision to these children and young adults."

Under terms of the agreement, Eluminex will make an upfront payment and earnout payments to Retinagenix for the purchase of the assets. The earnout payments to Retinagenix shall include (a) clinical, regulatory, and commercial milestone payments and (b) payments based upon worldwide net sales of products and the sale or use of priority review vouchers. The closing of this transaction is subject to certain customary conditions.

"Our focus at Retinagenix has been to see the zuretinol clinical program advance and for the drug to obtain regulatory approval in order to provide a safe, oral therapy for children and adults with these debilitating retinal

degenerations. We believe Eluminex Biosciences is uniquely situated to complete the zuretinol development program and efficiently gain global regulatory approval for the compound," said David Saperstein, MD, Chief Medical Officer of Retinagenix.

About the Zuretinol Retinal Rare Pediatric Disease Program

The Eluminex zuretinol program (EB-109) is a clinical stage, novel, oral therapy for the treatment of a rare form of childhood blindness in patients with LCA or RP caused by mutations of the *RPE65* or *LRAT* gene. EB-109 is regulated as a small molecule pharmaceutical product and is anticipated to enter a global Phase 2b/3 pediatric study in 2H 2022 to confirm its efficacy and safety. Orally administered zuretinol has been previously evaluated in 144 human subjects in 8 clinical studies, including healthy subjects, patients with recessive *RPE65/LCA*[1,2], autosomal dominant *RPE65*[1,2], and adults with early age-related macular degeneration (AMD) with poor night vision[3], which has demonstrated that zuretinol appears safe and well-tolerated and can rapidly improve visual function.

The zuretinol program was granted Orphan Drug Designation by the United States Food and Drug Administration (FDA) and the European Medicine Agency (EMA). It has also received FDA Rare Pediatric Disease and Fast Track designation and is eligible for a Rare Pediatric Disease Priority Review Voucher (PRV) which is transferable and allows the holder Priority Review (6 months) instead of the standard 10 months for any future regulatory submission.

About LCA and RP Caused by *RPE65/LRAT* Mutations

Retinitis pigmentosa (RP) is one of the most common forms of inherited retinal degeneration and Leber congenital amaurosis (LCA) is a severe inherited form of retinal degeneration, each have a prevalence of approximately 1 in 3,000-4,000 and 1 in 33,000 live births worldwide, respectively. About 5% of RP patients and 10% of LCA patients have mutations in the *LRAT* or *RPE65* genes.

Mutations in *RPE65* and *LRAT* cause both RP and LCA in humans where two key enzymes of the visual cycle, retinoid isomerase *(RPE65)* and lecithin:retinol acyltransferase *(LRAT),* are missing which cause severe impairment in rod photoreceptor function. These patients suffer from severe vision loss or eventual total blindness.

Currently, the only approved treatment for patients with *RPE65* mutations is LUXTURNA® (voretigene neparvovec-rzyl) in the United States and the European Union. There are no approved treatments for *LRAT* mutations. LUXTURNA® is a gene therapy administered through subretinal injection into

the diseased eye. Besides the high cost and the need to perform surgery and inject each eye separately, only about 15-25% of the injected retina is treated which leads to limited vision recovery. Long-term safety follow-up studies have reported adverse reactions including dyschromatopsia, glare, and probable surgery-related macular scar and thinning.[4] Therefore, an unmet needs exist for non-surgical, bilateral treatment of retinal dystrophies secondary to *RPE65/LRAT* mutations at improved cost.

About Zuretinol for Impaired Dark Adaptation (Night Blindness) in Early Dry AMD

Dark adaptation (night vision) is the ability for the eye to adjust from seeing in the light to seeing in dark or dim light environments. Research shows this function is compromised from the earliest stages of AMD and impairment increases as the disease progresses. Impaired dark adaptation (also referred to as night blindness or nyctalopia) has been observed in AMD at least three years before drusen are visible and there is a positive correlation between the degree of dark adaptation impairment and severity of AMD.[5,6]

Future developments for zuretinol include potential treatment for impaired dark adaption in adult patients due to early AMD. A prior multicenter, placebo-controlled Phase 2a study of oral zuretinol in adult patients (N=43) with impaired dark adaptation in early-stage AMD demonstrated evidence of rapidly improved dark adaptation, glare recovery, and low luminance, low contrast best corrected visual acuity in patients receiving zuretinol compared to placebo and appeared safe and well-tolerated and provides support for further clinical development.[3]

About Eluminex Biosciences

Eluminex Biosciences is a privately-held clinical-stage biotechnology company focused on both global and regional development and commercialization of innovative therapeutics to fulfill unmet medical needs in the treatment and management of ophthalmic diseases. Eluminex is devoted towards innovating the next generation of first-in-class or best-in-class ocular therapeutics for vision-threatening or lifestyle-limiting ocular diseases.

In addition to the zuretinol program (EB-109), Eluminex has exclusively licensed global rights for the development and commercialization of an investigational clinical-stage biosynthetic cornea derived from recombinant human collagen Type III for the treatment of corneal blindness.

Eluminex is developing a pipeline of next generation protein therapeutics for retinal diseases (EB-101, EB-102, EB-105, and EB-107) including age-related

macular degeneration, macular edema, and diabetic retinopathy; these assets are wholly owned and developed by Eluminex.

The Eluminex global headquarters and research and development center are located in Suzhou BioBay Industrial Park, China, with a US-subsidiary located in the San Francisco Bay Area. Eluminex is supported by three premiere global life science venture funds: Lilly Asia Ventures, Hillhouse Capital, and Quan Capital.

For more information, please visit www.eluminexbio.com.

About Retinagenix Holdings, LLC

Retinagenix is a privately-held biotechnology company devoted to addressing the large and expanding unmet medical needs in genetically determined orphan diseases of the eye. Retinagenix was founded by Marco Northland, serial entrepreneur, and David Saperstein, MD, co-inventor of the technology behind the zuretinol program developed while Dr. Saperstein was at the University of Washington. Dr. Saperstein has been engaged in retina research for more than 30 years and is a practicing retinal surgeon.

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典晶生物宣布从 Retinagenix Holdings 公司收购其 Zuretinol 资产

- 典晶生物获得用于治疗罕见型儿童失明症的 Zuretinol 的全球独占研发和商业化权益
- 该临床阶段的同类首创新药如果获批上市，将成为全球首个针对由 RPE65 或 LRAT 基因突变引起的莱伯氏先天性黑朦（LCA）及视网膜色素变性（RP）的口服药
- 该项目已被 FDA 授予罕见儿科疾病资格及快速审评通道，并有资格获得儿科罕见疾病优先审查凭证
- 未来 Zuretinol 将有机会用于治疗成人由早期干性年龄相关性黄斑病变（AMD）引起的暗适应受损的适应症

2022 年 1 月 19 日，典晶生物宣布从 Retinagenix Holdings 公司（一家位于美国华盛顿州西雅图的眼科公司）收购 Zuretinol 资产，包括其全球独占研发和商业化权益。Zuretinol 是一项处于临床阶段的用于治疗由 RPE65 或 LRAT 基因突变导致的莱伯氏先天性黑朦（LCA）或视网膜色素变性（RP）的同类首创口服疗法。

典晶生物首席医学官 Charles Semba 博士表示：“将 Zuretinol 加入到我们不断拓宽的视网膜疾病产品管线中进一步证实了我们为全球患有威胁视力的疾病患者开发创新疗法的承诺。目前世界上唯一获批治疗由 RPE65 及 LRAT 基因突变引起的 LCA 及 RP 的疗法是基因治疗，它需要患病儿童双眼分别进行手术并且只能治疗到视网膜的一小部分。而 Zuretinol 有希望能够同时治疗双眼及整个视网膜，它既可以作为单一疗法，也可以辅助现有的基因疗法来恢复患病儿童和青年人的视力。”

Retinagenix 首席医学官 David Saperstein 博士表示：“我们一直致力于推进 Zuretinol 的临床开发，并使该药最终获得批准，为患有这类罕见视网膜变性型疾病的儿童和成年人提供安全的口服疗法。我们相信典晶生物能够利用其独有的优势来完成 Zuretinol 的开发计划并获得全球注册批准。”

关于 Zuretinol 儿童罕见视网膜疾病项目

典晶生物 Zuretinol 项目（EB-109）是治疗由 RPE65 或 LRAT 基因突变引起的儿童罕见失明症 LCA 或 RP 的临床阶段创新口服药物。EB-109 是一种小分子药物，预计将于 2022 年下半年进入全球 2b/3 期儿童临床研究，以确认其有效性和安全性。在先前的 8 项临床研究中，Zuretinol 口

服制剂已经在 144 例受试者中进行了测试，包括健康受试者，隐性 RPE65/LCA 患者，常染色体显性 RPE65 患者，以及暗适应受损的早期 AMD 患者。这些研究均表明 Zuretinol 具有良好的安全性，耐受性和显著的临床疗效，能够快速改善患者的视觉功能。

Zuretinol 项目已被美国 FDA 和 EMA 认定为孤儿药，还被 FDA 授予了儿科罕见疾病资格及快速审评通道，并有资格获得儿科罕见疾病优先审查凭证。

关于由 RPE65 和 LRAT 基因突变引起的 LCA 及 RP

视网膜色素变性（RP）是最常见的遗传性视网膜变性疾病，而莱伯氏先天性黑朦（LCA）是一种严重的遗传性视网膜变性。在全球范围内，约 3,000–4,000 名新生儿中就有 1 例患有 RP，约 33,000 名新生儿中有 1 例患有 LCA，大约 5%的 RP 和 10%的 LCA 患者有 LRAT 或 RPE65 基因突变。

RPE65 和 LRAT 突变会导致视觉周期中的两种关键酶-视黄醇异构酶及卵磷脂:视黄醇酰基转移酶的缺失，导致视杆感光功能严重受损，这些患者患有严重的视力下降或最终完全失明。

目前，LUXTURNA® (voretigene neparvovec-rzyl) 是在美国和欧洲唯一获得批准能够治疗 RPE65 基因突变的药物。世界上还没有获得批准的用于治疗 LRAT 基因突变的方法。除了高昂的成本和每只眼睛必须单独接受注射手术外，经过注射治疗的视网膜只有约 15-25%的面积能够恢复部分的视力。长期随访的临床研究还发现 LUXTURNA® 会造成色光障碍、眩光、以及手术导致的黄斑瘢痕和黄斑变薄等不良反应。因此，对于价格合理又能够同时进行双眼治疗的非手术疗法是未满足的临床需求。

关于 Zuretinol 治疗因早期干性黄斑病变引起的暗适应受损（夜盲症）

暗适应是眼睛从光亮环境适应黑暗或昏暗环境的一种调节能力。研究表明，在 AMD 最早期阶段这一功能就开始受损，随着病情发展，这一功能损害也逐渐加剧。AMD 患者从玻璃疣出现前至少三年就已经能够观察到暗适应受损现象（通常也称为夜盲症），并且暗适应的受损程度与 AMD 的严重程度成正相关。

Zuretinol 未来有可能被用于治疗成人因早期 AMD 引起的暗适应受损。先前一项针对早期 AMD 暗适应受损的成年患者（N=43）的多中心、安慰剂对照的 2a 期临床研究表明：与安慰剂对照组相比，口服 Zuretinol 的受试者暗适应能力、眩光恢复，低亮度、低对比度最佳矫正视力都迅速得到改善，并且结果显示 Zuretinol 具有良好的安全性及耐受性，支持进一步的临床研究。

关于典晶生物

典晶生物是一家处于临床阶段的私营生物技术公司，专注于创新疗法在全球的开发和商业化，以满足眼科疾病治疗和管理方面未满足的需求。典晶生物致力于开发同类首个或者同类最优的眼科治疗方法，减少眼科疾病对患者视力的威胁和由此带来的生活不便。

除了 Zuretinol 项目（EB-109），典晶生物不久前还获得了用于治疗角膜盲的重组人胶原蛋白生物合成角膜独家全球开发和商业化权力。

典晶生物全球总部和研发中心位于中国苏州生物医药产业园区，美国子公司位于加州旧金山湾区。典晶生物获得了三家顶级风险投资基金的支持：礼来亚洲基金、高瓴创投和泉创资本。如需了解更多信息，请访问 www.eluminexbio.com。

关于 Retinagenix Holdings 公司

Retinagenix Holdings 是一家私营生物技术公司，专注于因基因缺陷而导致的眼科孤儿病。公司由连续创业者 Marco Northland 和 Zuretinol 核心技术的共同发明者 David Saperstein 博士创立。Saperstein 博士从事视网膜研究 30 多年，是一名执业视网膜外科医生，Zuretinol 项目的核心技术是他在华盛顿大学期间开发的。