REGENXBIO Announces Additional Positive Interim Data from Trials of RGX-314 for the Treatment of Wet AMD

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- *Company announced positive interim data from and the expansion of Phase II AAVIATE® trial of RGX-314 for the treatment of wet AMD using suprachoroidal delivery*
    - *RGX-314 continues to be well tolerated in 85 patients from Cohorts 1-5 with no drug-related serious adverse events*
    - *Meaningful reduction in treatment burden at six months across all dose levels, 85% reduction in treatment burden observed at third dose level*
    - *67% of patients in Cohort 4 were injection-free*
    - *No meaningful differences in outcomes at six months for patients who are NAb positive*
    - *Phase II trial expanded to include new cohort at third dose level with short-course prophylactic ocular steroids following RGX-314 administration*
- *Positive interim data presented at the AAO Annual Meeting from the Phase I/IIa Long-term Follow-up study of RGX-314 for the treatment of wet AMD using subretinal delivery*
    - *RGX-314 continues to be well-tolerated and demonstrates long-term, durable treatment effect up to four years*
    - *Two pivotal trials, ATMOSPHERE® and ASCENT™, are active and enrolling patients*
    - *Pivotal trials are expected to support BLA submission in 2024*
- *New interim data from Phase II ALTITUDE® trial of RGX-314 for the treatment of diabetic retinopathy using suprachoroidal delivery expected at the Retina Society 55th Annual Scientific Meeting in November*
- *Conference call Monday, October 3 at 8:30 a.m. ET*

ROCKVILLE, Md, Oct. 3, 2022 (PRNewswire) – REGENXBIO Inc. (Nasdaq: RGNX) today announced a program update from its ongoing clinical investigation of RGX-314 for the treatment of wet AMD, a leading cause of vision loss globally.

REGENXBIO announced positive interim data from the Phase II AAVIATE® trial of RGX-314 for the treatment of wet AMD using suprachoroidal delivery. REGENXBIO also presented positive interim data from the Phase I/IIa long-term follow-up (LTFU) study of RGX-314 for the treatment of wet AMD using subretinal delivery at the American Academy of Ophthalmology (AAO) annual meeting this past weekend in Chicago.

"Today's announcements come nearly a year into our collaboration with AbbVie to advance RGX-314 in wet AMD and other retinal diseases. These new subretinal and suprachoroidal data highlight the potential impact of RGX-314 for the millions of patients facing vision loss from wet AMD," said Kenneth T. Mills, President and Chief Executive Officer of REGENXBIO. "I am pleased with the continued progress on and momentum for these programs. We remain on track to submit a BLA for RGX-314 in 2024, and we expect to provide an update on the ALTITUDE trial of RGX-314 for the treatment of diabetic retinopathy using suprachoroidal delivery at the upcoming Retina Society Meeting in November."

Data Summary and Safety Update for the Phase II AAVIATE Trial of RGX-314 using Suprachoroidal Delivery
The Phase II AAVIATE trial of RGX-314 for the treatment of wet AMD using in-office suprachoroidal delivery continues to show positive interim results. AAVIATE is a multi-center, open-label, randomized, active-controlled, dose-escalation trial that is evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314. The primary endpoint of the trial is mean change in vision in patients dosed with RGX-314, as measured by best corrected visual acuity (BCVA) at Week 40 from baseline, compared to patients receiving monthly injections of ranibizumab. Other endpoints include mean change in central retinal thickness (CRT) and number of anti-vascular endothelial growth factor (anti-VEGF) intravitreal injections received following administration of RGX-314.

As of August 1, 2022, RGX-314 suprachoroidal delivery was reported to be well tolerated across 85 patients dosed in Cohorts 1-5. Fifteen SAEs were reported, none of which were considered related to RGX-314. For the total group of Cohorts 1-4 (n=65), all common treatment emergent adverse events (TEAEs) through 6 months in the study eye were mild or moderate and included conjunctival hemorrhage, increased intraocular pressure, episcleritis, and conjunctival hyperemia. Mild intraocular inflammation was reported at similar incidence in the first and second dose levels, with an

increase in incidence in mild to moderate inflammation seen at the third dose level (Cohort 4). All intraocular inflammation resolved with topical corticosteroids.

Patients treated in the RGX-314 arms and the ranibizumab control arm both continue to demonstrate stable BCVA and CRT at 6 months. In addition, a meaningful reduction in anti-VEGF treatment burden following administration of RGX-314 compared to mean annualized injection rate during the 12 months prior to administration was observed and ranged from -63.8% to -84.7% across all cohorts. The highest reduction in treatment burden was observed in the third dose level, with patients receiving a mean of 1.3 injections over six months following administration of RGX-314, which represents an 84.7% reduction in anti-VEGF treatment burden. Ten out of 15 patients (67%) in the third dose level received no anti-VEGF injections over six months following RGX-314 administration. In these patients, visual acuity and CRT was observed to be stable over six months.

Additionally, the interim data from the second dose level (Cohorts 2 and 3) suggests there is no meaningful difference in safety and vision outcomes for patients who are neutralizing antibody (NAb) positive.

Phase II AAVIATE Trial Expansion to Cohort 6
REGENXBIO announced today that the AAVIATE study has expanded, and an additional cohort (Cohort 6) will be enrolled to evaluate RGX-314 at the third dose level of $1x10^{12}$ GC/eye with a short course of prophylactic ocular steroids to evaluate the ability to prevent or reduce the occurrence of the mild to moderate intraocular inflammation seen to date. Patients will be enrolled in Cohort 6 regardless of NAb status.

"We are pleased to share updated data from the AAVIATE trial, including new 6-month data from Cohorts 1-4 which provides continued evidence of the emerging clinical profile of RGX-314 for the treatment of wet AMD using suprachoroidal delivery," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "RGX-314 continues to be well tolerated, with emerging evidence of treatment effect, including meaningful reduction in anti-VEGF treatment burden at all dose levels. We look forward to expanding this trial to further explore the third dose level."

Data Summary from Phase I/IIa Long-term Follow-up Study of RGX-314 using Subretinal Delivery
The Phase I/IIa study evaluated RGX-314 in 42 patients with wet AMD using subretinal delivery and was designed as an open label, dose escalation study evaluating five doses of RGX-314 over two years. Dose dependent increases in treatment effect were observed, and doses similar to those used in Cohort 3 and Cohort 4 of the Phase I/IIa trial were advanced into the ongoing pivotal trials, ATMOSPHERE and ASCENT. After the Phase I/IIa study's completion, patients were encouraged to enroll into a long-term follow-up study for up to five years after RGX-314 administration. Data presented at AAO highlights the results of the 16 (out of 18) patients from Cohorts 3 and 4 who enrolled in the LTFU study, with data now out to 4 years and 3 years, respectively. Data from this study demonstrating that RGX-314 continues to be well-tolerated with long-term, durable treatment effect up to four years is expected to support the anticipated BLA filing for RGX-314 in 2024.

As of August 29, 2022, RGX-314 continues to be generally well-tolerated in the long-term follow-up study (n=37). A total of nine serious adverse events (SAEs) were reported in four patients, none of which were considered related to RGX-314. No new drug-related ocular AEs were reported in the long-term follow-up study for Cohorts 3 and 4. One patient in Cohort 5 experienced a significant decrease of vision during the long-term follow-up study who had macular pigmentary changes after a superior bleb in the Phase I/IIa trial.

Patients treated with RGX-314 continue to demonstrate a long-term, durable treatment effect in Cohort 3 up to 4 years and Cohort 4 up to three years. Stable to improved visual acuity was observed, with a mean BCVA of +12 letters from baseline at four years for Cohort 3 patients and -5 letters from baseline at three years for Cohort 4 patients following RGX-314 administration.

Patients also demonstrated meaningful long-term reductions in anti-VEGF treatment burden following administration of RGX-314. Patients in Cohort 3 received a mean annualized rate of 2.4 injections through 4 years following administration of RGX-314 (versus 6.8 injections in the 12 months prior to treatment), representing a 67.0% reduction in mean annualized injection rate. Patients in Cohort 4 received a mean annualized rate of 4.4 injections through 3 years following administration of RGX-314 (versus 10.2 injections in the 12 months prior to treatment), representing a 58.4% reduction in mean annualized injection rate.

"These positive interim data from the long-term follow-up and AAVIATE trials continue to reinforce the potential clinical benefit of a one-time administration of RGX-314 in the overall management of patients with neovascular AMD," said Arshad M. Khanani, M.D., M.A., FASRS, Director of Clinical Research at Sierra Eye Associates, Reno, NV. "I am extremely encouraged by this long-term data up to four years showing durable treatment effect and the potential of RGX-314 to meaningfully reduce injection burden for patients while maintaining vision outcomes. I look forward to the further investigation of RGX-314 in Cohort 6 of the AAVIATE trial, as in-office suprachoroidal delivery has the potential to be an important treatment option for patients."

These study findings are available under the Presentations & Publications page in the Media section of REGENXBIO's website located at www.regenxbio.com.

Conference Call
In connection with this announcement, REGENXBIO will host a conference call and webcast today at 8:30 a.m. ET to discuss the new, interim update from the ongoing Phase II AAVIATE® trial of RGX-314 for the treatment of wet AMD using suprachoroidal delivery. Listeners can register for the webcast via this link. Analysts wishing to participate in the question and answer session should use this link. A replay of the webcast will be available via the Company's investor website approximately two hours after the call's conclusion. Those who plan on participating are advised to join 15 minutes prior to the start time.

About the AAVIATE® Trial
The multi-center, open-label, randomized, active-controlled, dose-escalation Phase II AAVIATE trial is evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314 in patients with wet AMD using the Clearside SCS Microinjector®. Twenty patients in Cohort 1 were randomized to receive RGX-314 at a dose level of $2.5x10^{11}$ genomic copies per eye (GC/eye) through one injection versus monthly 0.5 mg ranibizumab intravitreal injection at a 3:1 ratio. Twenty patients in Cohort 2 were randomized to receive RGX-314 at a dose level of $5x10^{11}$ GC/eye through two injections versus monthly 0.5 mg ranibizumab intravitreal injection at a 3:1 ratio. Cohort 3 is evaluating RGX-314 at the same dose level as Cohort 2 in 20 patients who are NAb positive. Cohort 4 is evaluating RGX-314 in 15 patients at a dose level of $1x10^{12}$ GC/eye and Cohort 5 is evaluating the same dose level of RGX-314 in 20 patients who are NAb positive. Cohort 6 is evaluating patients at the same dose level as Cohorts 4 and 5 and includes a short course of prophylactic steroids following administration of RGX-314.

About RGX-314
RGX-314, being developed in collaboration with AbbVie, is being investigated as a potential one-time treatment for wet AMD, diabetic retinopathy, and other chronic retinal conditions. RGX-314 consists of the NAV® AAV8 vector, which encodes an antibody fragment designed to inhibit vascular endothelial growth factor (VEGF). RGX-314 is believed to inhibit the VEGF pathway by which new, leaky blood vessels grow and contribute to the accumulation of fluid in the retina.

REGENXBIO is advancing research in two separate routes of administration of RGX-314 to the eye, through a standardized subretinal delivery procedure as well as delivery to the suprachoroidal space. REGENXBIO has licensed certain exclusive rights to the SCS Microinjector® from Clearside Biomedical, Inc. to deliver gene therapy treatments to the suprachoroidal space of the eye.

About Wet AMD
Wet AMD is characterized by loss of vision due to new, leaky blood vessel formation in the retina. Wet AMD is a significant cause of vision loss in the United States, Europe and Japan, with up to 2 million people living with wet AMD in these geographies alone. Current anti-VEGF therapies have significantly changed the landscape for treatment of wet AMD, becoming the standard of care due to their ability to prevent progression of vision loss in the majority of patients. These therapies, however, require life-long repeated intraocular injections to maintain efficacy. Due to the burden of treatment, it is difficult for patients to adhere to frequent injections, which can lead to a decline in vision over time.

About REGENXBIO Inc.
REGENXBIO is a leading clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy. REGENXBIO's NAV Technology Platform, a proprietary adeno-associated virus (AAV) gene delivery platform, consists of exclusive rights to more than 100 novel AAV vectors, including AAV7, AAV8, AAV9 and AAVrh10. REGENXBIO and its third-party NAV Technology Platform Licensees are applying the NAV Technology Platform in the development of a broad pipeline of candidates, including late-stage and commercial programs, in multiple therapeutic areas. REGENXBIO is committed to a "5x'25" strategy to progress five AAV Therapeutics from our internal pipeline and licensed programs into pivotal-stage or commercial products by 2025.

Forward-Looking Statements
This press release includes "forward-looking statements," within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements express a belief, expectation or intention and are generally accompanied by words that convey projected future events or outcomes such as "believe," "may," "will," "estimate," "continue," "anticipate," "assume," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would" or by variations of such words or by similar expressions. The forward-looking statements include statements relating to, among other things, REGENXBIO's future operations and clinical trials. REGENXBIO has based these forward-looking statements on its current expectations and assumptions and analyses made by REGENXBIO in light of its experience and its perception of historical trends, current conditions and expected future developments, as well as other factors REGENXBIO believes are appropriate under the circumstances. However, whether actual results and developments will conform with REGENXBIO's expectations and predictions is subject to a number of risks and uncertainties, including the timing of enrollment, commencement and completion and the success of clinical trials conducted by REGENXBIO, its licensees and its partners, the timing of commencement and completion and the success of preclinical studies conducted by REGENXBIO and its development partners, the timely development and launch of new products, the ability to obtain and maintain regulatory approval of product candidates, the ability to obtain and maintain intellectual property protection for product candidates and technology, trends and challenges in the business and markets in which REGENXBIO operates, the size and growth of potential markets for product candidates and the ability to serve those markets, the rate and degree of acceptance of product candidates, the impact of the COVID-19 pandemic or similar public health crises on REGENXBIO's business, and other factors, many of which are beyond the control of REGENXBIO. Refer to the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of REGENXBIO's Annual Report on Form 10-K for the year ended December 31, 2021, and comparable "risk factors" sections of REGENXBIO's Quarterly Reports on Form 10-Q and other filings, which have been filed with the U.S. Securities and Exchange Commission (SEC) and are available on the SEC's website at www.sec.gov. All of the forward-looking statements made in this press release are expressly qualified by the cautionary statements contained or referred to herein. The actual results or developments anticipated may not be realized or, even if substantially realized, they may not have the expected consequences to or effects on REGENXBIO or its businesses or operations. Such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Readers are cautioned not to rely too heavily on the forward-looking statements contained in this press release. These forward-looking statements speak only as of the date of this press release. Except as required by law, REGENXBIO does not undertake any obligation, and specifically declines any obligation, to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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