REGENXBIO Announces Additional Positive Interim Phase I/IIa and Long-Term Follow-Up Data of RGX-314 for the Treatment of Wet AMD

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- *RGX-314 using subretinal delivery continues to be generally well-tolerated at all dose levels*
- *Positive interim update from Cohorts 4 and 5 at 1.5 years after RGX-314 administration*
  - *Durable treatment effect observed with stable visual acuity, decreased retinal thickness, and reductions in anti-VEGF injection burden*
- *Long-term, durable treatment effect over three years demonstrated in Cohort 3*
  - *Mean improvement in vision and stable retinal thickness*
  - *50% of patients (3/6) remain anti-VEGF injection-free over three years; 67% of patients (4/6) are anti-VEGF injection-free from nine months to three years*
- *ATMOSPHERE™, the first of two planned pivotal trials for RGX-314, is active and enrolling*

REGENXBIO Inc. (Nasdaq: RGNX) reported at the Angiogenesis, Exudation, and Degeneration 2021 conference additional positive interim data from Cohorts 4 and 5 of its RGX-314 Phase I/IIa trial for the treatment of wet age-related macular degeneration (wet AMD), and Cohort 3 of its Long-Term Follow-Up (LTFU) study. RGX-314 is a potential best-in-class, one-time gene therapy for the treatment of wet AMD.

"The continued durability of treatment effect up to three years after RGX-314 administration highlights the potential of RGX-314 as a one-time treatment option for patients with wet AMD. The results from the Phase I/IIa trial of RGX-314 using subretinal delivery have informed the key design elements of our pivotal program, in which we plan to conduct two randomized, well-controlled clinical trials, enrolling approximately 700 patients total," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO.

"I am excited about this data out to three years, which demonstrates that one-time treatment with RGX-314 has the potential to result in long-term stability to improvement of visual acuity outcomes and retinal anatomy, while alleviating treatment burden," said Allen C. Ho, M.D., Director of Retina Research at Wills Eye Hospital and Mid Atlantic Retina and investigator surgeon in the RGX-314 clinical trials. "In our practice, and as reported by multiple real-world studies, we see many patients losing vision due to lack of compliance with standard of care, which requires frequent anti-VEGF injections. I look forward to further evaluating the effects of RGX-314 in ATMOSPHERE^{TM}, the first pivotal trial of a gene therapy for the treatment of wet AMD."

Study Design and Safety Update from Phase I/IIa Trial of RGX-314 for the Treatment of Wet AMD Using Subretinal Delivery

In the Phase I/IIa trial of RGX-314, 42 patients with severe wet AMD requiring frequent anti-vascular endothelial growth factor (anti-VEGF) injections were treated across five dose cohorts, with doses ranging from $3x10^9$ GC/eye to $2.5x10^{11}$ GC/eye.

As of January 22, 2021, RGX-314 continued to be generally well-tolerated across all cohorts, with 20 serious adverse events (SAEs) reported in 13 patients, including one possibly drug-related SAE of significant decrease in vision in Cohort 5. The most common nonserious adverse events in the eye were generally assessed as mild (87%). These included post-operative conjunctival hemorrhage (69% of patients), post-operative inflammation (36% of patients), eye irritation (17% of patients), eye pain (17% of patients), and post-operative visual acuity reduction (17% of patients). In 67% of patients across all cohorts, and in 83% of patients in Cohorts 3 through 5, retinal pigmentary changes were observed on imaging, the majority of which were in the peripheral inferior retina. Retinal hemorrhage was observed in 26% of patients and is an anticipated event in patients with severe wet AMD. There have been no reports of clinically-determined immune responses, drug-related ocular inflammation, or post-surgical inflammation beyond what is expected following routine vitrectomy.

Summary of Data for Cohorts 4 and 5

Today's update includes data from Cohorts 4 and 5 as of January 22, 2021. Each cohort enrolled 12 patients each at doses of $1.6x10^{11}$ GC/eye and $2.5x10^{11}$ GC/eye, respectively.

Patients in Cohorts 4 and 5 at 1.5 years after administration of RGX-314 demonstrated stable visual acuity with a mean Best Corrected Visual Acuity (BCVA) change of +1 letters and -1 letters from baseline, respectively, as well as decreased central retinal thickness (CRT), with a mean change of -46 µm and -93 µm, respectively.

There was a meaningful reduction in anti-VEGF treatment burden in both Cohorts 4 and 5 compared to the mean annualized injection rate during the 12 months prior to RGX-314 administration. Patients in Cohort 4 received a mean of 4.4 injections over 1.5 years following administration of RGX-314, a 58.3% reduction in anti-VEGF treatment burden. Patients in Cohort 5 received a mean of 1.7 injections over 1.5 years following administration of RGX-314, a reduction in anti-VEGF treatment burden of 81.2%.

In Cohort 4, four out of 12 (33%) patients have received no anti-VEGF injections after six months following RGX-314 administration and demonstrated

a mean BCVA change from baseline of +2 letters at 1.5 years. Eight out of 11 (73%) patients have received no anti-VEGF injections after six months following RGX-314 administration and demonstrated a mean BCVA change from baseline of -2 letters at 1.5 years.

Summary of Long-Term Follow-Up (LTFU) Study Data

Following the Phase I/IIa trial, patients are encouraged to enroll in a LTFU study to assess safety and efficacy up to five years after RGX-314 administration. Patients in the LTFU study have scheduled visits every six months for the first year and then annual visits until the end of the study. Patient management is per physician discretion. Data collected during the scheduled study visits include safety, BCVA, and CRT. In addition, chart reviews are conducted at each scheduled study visit to collect the number of retina specialist visits and anti-VEGF injections each patient has received since the prior scheduled study visit.

As of January 22, 2021, RGX-314 continued to be generally well-tolerated in patients enrolled in the LTFU study, with no new drug-related ocular adverse events reported.

All six patients from Cohort 3 of the Phase I/IIa trial enrolled in the LTFU study, and long-term treatment effect was demonstrated over three years. These patients demonstrated a mean BCVA improvement of +12 letters from baseline at three years. Retinal anatomy as measured by machine-read CRT remained stable at three years compared to the two-year timepoint.

Patients also demonstrated long-term reductions in anti-VEGF treatment burden over three years with a mean annualized rate of 2.4 anti-VEGF injections after administration of RGX-314, which is a reduction of 66.7% from the mean annualized injection rate during the 12 months prior to administration of RGX-314. Three out of six (50%) patients received no anti-VEGF injections over three years following one-time administration of RGX-314. Four out of six (67%) patients have received no anti-VEGF injections from nine months to three years after RGX-314 administration. The four patients who did not receive anti-VEGF injections after nine months demonstrated a mean BCVA improvement from baseline of +11 letters at three years.

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 intraocular injections, typically repeated every four to 12 weeks in frequency, to maintain efficacy. Due to the burden of treatment, patients often experience a decline in vision with reduced frequency of treatment over time.

About RGX-314

RGX-314 is being developed 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 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 the Phase I/IIa Clinical Trial of RGX-314 and Long-Term Follow-Up Study

RGX-314 is being evaluated in a Phase I/IIa, multi-center, open-label, multiple-cohort, dose-escalation study in adult patients with wet AMD in the United States. The study includes patients previously treated for wet AMD who are responsive to anti-VEGF therapy. The study is designed to evaluate five escalating doses of RGX-314, with six patients in the first three dose cohorts and 12 patients in the fourth and fifth dose cohorts. Patients were enrolled into all dose cohorts independent of their neutralizing antibody titers to AAV and did not receive prophylactic immune suppressive oral corticosteroid therapy before or after administration of RGX-314. The primary endpoint of the study is safety at 6 months following administration of RGX-314. Secondary endpoints include visual acuity, retinal thickness on SD–OCT, ocular RGX-314 protein expression, and the need for additional anti-VEGF therapy. Following completion of the primary study period, patients enter a follow-up period and will continue to be assessed until week 106 for long-term safety and durability of effect. After completion of the Phase I/IIa clinical trial, patients are encouraged to enter a Long-Term Follow-Up study to continue to follow safety and efficacy for a total of 5 years following administration of RGX-314.

About ATMOSPHERE™

ATMOSPHERE is a multi-center, randomized, active-controlled trial to evaluate the efficacy and safety of a single-administration of RGX-314 versus standard of care in patients with wet AMD. The trial is designed to enroll 300 patients at a 1:1:1 ratio across two RGX-314 dose arms ($6.4x10^{10}$ genome copies (GC)/eye and $1.3x10^{11}$ GC/eye delivered subretinally) and an active control arm of monthly intravitreal injections of ranibizumab (0.5 mg/eye). The primary endpoint of the trial is non-inferiority to ranibizumab based on change from baseline in Best Corrected Visual Acuity (BCVA) at 54 weeks. Secondary endpoints of the trial include safety and tolerability, change in central retinal thickness (CRT) and need for supplemental anti-VEGF injections. Patient selection criteria will include patients with wet AMD who are responsive to anti-VEGF treatment and will be independent of preexisting neutralizing antibody status. Patients will not receive prophylactic immune suppressive corticosteroid therapy before or after administration of RGX-314. The trial will be conducted at approximately 60 clinical sites based in the United States, with over 100 retinal surgeons.

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 in multiple therapeutic areas.

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," "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 accurately predict how long REGENXBIO's existing cash resources will be sufficient to fund its anticipated operating expenses, 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, 2019, 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. 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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