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August 22, 2022

Dear Stockholder:

This past year provided new insight into the clinical development of RGN-259, our product candidate for dry eye disease (DED) and neurotrophic keratitis (NK). We would like to take this opportunity to briefly update you on these events and our plans for the next twelve to eighteen months, as well as our regulatory and operational plans with respect to RGN-352. As always, we reserve the right to modify our goals and expectations from time to time in accordance with clinical development of our product candidates, FDA interaction, access to capital markets, and the general climate in the pharmaceutical industry.

RGN-259 Clinical Trials

Background

As discussed in last year's Letter to Stockholders, the development of RGN-259 for ocular diseases in North America is being sponsored by ReGenTree, LLC, a U.S. joint venture between RegeneRx and HLB Therapeutics (formerly GtreeBNT), our Korean partner. HLBT is responsible for operating ReGenTree and funding its ophthalmic clinical development program. We have also licensed the rights to RGN-259 to HLBT for South Korea and several additional countries throughout Asia. Additionally, we licensed RGN-259 for development in Greater China to Lee's Pharma, a Hong Kong-based biopharmaceutical company, which subsequently licensed the product candidate to Zhaoke Ophthalmology in the territory

To market a drug or biologic specifically for the treatment of dry eye disease in the U.S., the FDA typically requires both a sign and symptom of DED to be improved by a statistically significant margin in a series of well-controlled clinical trials. A sign can be one of several assessments such as corneal staining (quite common), which is assessed by using fluorescein to temporarily stain the cornea to indicate damage or reduction of damage to the cornea.

Likewise, a symptom can be one of several assessments such as burning, stinging, or eye grittiness. Various models are used to assess symptoms, or patient discomfort, such as the Ocular Surface Disease Index (OSDI) and other patient questionnaires related to ocular discomfort.

In March 2020, Tβ4 was reclassified from a new drug to a biologic, requiring a Biologics License Application (BLA), rather than a New Drug Application (NDA) for marketing approval. The differences in these regulatory classifications have more to do with control of manufacturing processes related to biologics. We believe we are in an excellent position regarding the manufacturing controls and processes for RGN-259 and that this reclassification should not materially affect our regulatory path going forward. Moreover, since Tβ4 is now classified as a biologic, it is eligible to receive 12 years of market exclusivity under a BLA, rather than 6 years under an NDA, upon first marketing approval.

Dry Eye Disease Clinical Trials

The ARISE clinical trials are a series of three phase 3 clinical trials in over 1,600 patients, conducted in multiple medical centers across the U.S., assessing RGN-259 for the treatment of dry eye disease. As part of the process to fully understand patient data and the effects of RGN-259 compared to placebo we evaluated various subgroups of DED patients within ARISE-3 and pooled the data from all three ARISE clinical trials. Pooled data combines the patient data from all ARISE trials to analyze the results, which may also be compared to the results of each individual trial.

The key results are:

(1) While the pre-specified co-primary endpoints were not met, ARISE-3 provided statistically significant improvements with RGN-259 in a specific and common dry eye symptom, ocular grittiness, compared to placebo:
    a. observed one week after treatment;
    b. observed two weeks after treatment;
    c. observed two weeks after treatment after dry eye patients were stressed in the CAE model; and
    d. In several questions using the ocular surface disease index scale (OSDI), a different symptom assessment methodology.

(2) In ARISE-3, outside of the prespecified endpoints, statistically significant differences were seen in central corneal fluorescein staining, a sign of dry eye, at two weeks after treatment with RGN-259 in a subpopulation of patients;

(3) In a pooled sub-population of all three ARISE trials, statistically significant sign differences were also seen in central corneal staining;

(4) In ARISE-2 and in the same patient population within the pooled group of all three ARISE trials, statistically significant differences were observed in inferior corneal fluorescein staining, another sign of dry eye, at two weeks after treatment with RGN-259;

(5) RGN-259 acts rapidly;

(6) RGN-259 continued to demonstrate that it is safe and well-tolerated in the treatment of dry eye.

The conclusions from these expanded analyses are that while RGN-259 did not meet the pre-specified co-primary endpoints with statistical significance, RGN-259 did demonstrated statistically significant improvements in both signs and symptoms of dry eye disease in various patient populations and after one and two weeks of treatment when measured across three phase 3 clinical trials in over 1,600 patients. The product candidate's excellent safety profile was also confirmed.

ReGenTree representatives met with the FDA in February 2022 to discuss a potential BLA submission for RGN-259 for dry eye disease. The FDA determined that the clinical work to date did not reach the pre-specified co-primary endpoints required for approval of a biologics license. Therefore, ReGenTree advises us that it planning to apply for SPA (Special Protocol Assessment) to the FDA around October 2022. SPA is a program in which FDA specialists collaborate with a sponsor (ReGenTree) in setting up a clinical protocol

and statistical analysis plan. An agreed clinical trial design with FDA is binding and this program gives the sponsor and FDA a clear understanding of relevant trial criteria by participating together at this stage of the clinical trial protocol development. Once the SPA is in place, ReGenTree has advised us that it intends to conduct an ARISE-4 clinical trial in 2023.

NEUROTROPHIC KERATITIS CLINICAL TRIALS

Top line results for the Phase 3 NK trial (SEER-1) were reported in May 2020. The trial recruited, treated, and analyzed 18 patients. Six out of 10 patients in the RGN-259 treated group compared to 1 out of 8 patients in the placebo treated group achieved complete corneal healing in 4 weeks. In terms of the primary endpoint, "ratio of corneal wound healed patients after four weeks' administration," the statistical difference was slightly over 0.05 ($p = 0.0656$, Fisher's exact test), due to the limited number of patients in each group. We believe this strong trend likely would have reached a statistically significant p value of <0.05 had more patients been entered into the trial. When another statistical method was used to analyze the same primary endpoint (Chi square test), there was statistical significance, $p = 0.0400$, even with the limited number of patients.

In addition, in a pre-specified secondary endpoint evaluating corneal epithelial healing at day 43 (two weeks post-treatment) and the durability of RGN-259 treatment, there was a clear statistical difference using the Fisher's exact test, $p = 0.0359$. Several other efficacy parameters were either highly significant or strongly trending toward statistical significance in the RGN-259 group indicating the depth of patient response to RGN-259. These results demonstrated the efficacy of RGN-259 in NK, despite the small number of patients. As expected, the product candidate was well-tolerated and there were no safety issues.

While ReGenTree has previously spent the bulk of its efforts on dry eye clinical trials, due to the additional time necessary for clinical development of DED, ReGenTree is seeking to accelerating its effort in NK by scheduling two simultaneous phase 3 trials targeted to commence this Fall. Two positive phase 3 trials are necessary to meet FDA's requirement for marketing approval and conducting them simultaneously is aimed at accelerating our clinical development effort. ReGenTree will seek to confirm the corneal wound healing efficacy previously observed in SEER-1. The planned clinical trials, (SEER-2, SEER-3) are designed to enroll 60 patients in each study. To this end, ReGenTree has advised us it is retaining a contract research organization (CRO) and will start recruitment of patients before the end of 2022.

RGN-352 DEVELOPMENT

It has been our plan for several years to wait until the successful completion of RGN-259 clinical trials to take advantage of a potentially higher stock price and then raise capital for further development of RGN-352. However, now that RGN-259 will require additional time for development for DED and NK, we are re-evaluating opportunities to move forward with RGN-352.

Recent independent research has indicated that RGN-352 (injectable formulation of Tβ4 for systemic administration) may be a viable approach for treatment of certain acute systemic inflammatory disorders such as SIRS, ARDS, sepsis and COVID, among others. You may remember that researchers at Oak Ridge National Laboratories and their colleagues suggested that Tβ4 may be able to reduce damage caused by the intense inflammation, or cytokine storm, caused by COVID-19. Other research has shown that Tβ4 reduces scarring and down-regulates and suppresses inflammation in animal models. And still others have shown

that Tβ4 can alleviate acute lung inflammation and pulmonary fibrosis while low Tβ4 levels have been associated with higher acute kidney injury and mortality in human patients with sepsis, all suggesting that administering Tβ4 might reduce such damage. These recent findings have encouraged us to find ways to resume our RGN-352 program.

Therefore, we are renewing our efforts to finance phase 2 development of RGN-352 either through government grants, partnerships, and/or additional project-specific funding. We successfully completed a phase 1 dose-escalating trial in 80 healthy subjects some years ago that, along with more recently published scientific studies, provides the foundation we believe is required for initiating a phase 2a proof-of-concept clinical trial for an acute inflammatory indication. We will provide further detailed information as we move forward with our efforts in this area.

OPERATIONS

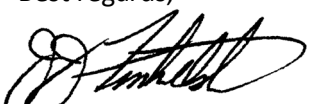
We stated in previous press releases, stockholder letters, and SEC filings that RegeneRx had limited capital and would be deploying its capital to maintain existing operations through the reporting of ARISE-3 results and the end of 2022, which is still the case. Our team continues to explore various financing possibilities for short-term and longer-term operations, including resuming development of RGN-352, depending on market conditions in the coming months. Our goal, of course, is to raise capital to develop our clinical assets and maximize stockholder value.

Last year, we filed several patents specifically related to the use of Tβ4 for the treatment of COVID and repair of organs damaged by the virus, as well as for other areas of research related to Tβ4. These patent applications, if granted, should extend and expand coverage of our areas of interest.

SUMMARY

We are evaluating ways to move forward with RGN-352 while the development of RGN-259 continues through our U.S. joint venture, ReGenTree LLC and our operating partner, HLB Therapeutics. Our other licensee, Zhaoke Ophthalmology, has previously informed us that it is moving forward with RGN-259 development in Greater China, although we have no current updates on timing. Research continues around the world with Tβ4 demonstrating its potential value in the treatment of many different diseases, all of which have commonalities of tissue and organ damage associated with inflammation. We look forward to continuing our work with Tβ4 and hope we will see positive results in the coming months.

Best regards,



J.J. Finkelstein
President & CEO

Allan L. Goldstein, Ph.D.
Chairman and Chief Scientific Advisor

Forward-Looking Statements

Any statements in this stockholder letter that are not historical facts are forward-looking statements made under the provisions of the Private Securities Litigation Reform Act of 1995. Any forward-looking statements involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Forward-looking statements in this stockholder letter include, but are not limited to, statements regarding our strategic and research partnerships, regulatory applications and approvals, the development and timing of clinical trials for our drug candidates, the use of our drug candidates to treat various conditions, our operating strategies, and our financial needs. The proposed clinical trials and costs to operate the Company during such trials, as well as the other forward-looking statements, are expectations and estimates based upon information obtained and calculated by the Company at this time and are subject to change. Moreover, there is no guarantee any of these trials will be successful or confirm previous clinical results. There also is no assurance that by the end of 2022 we can successfully raise the capital required to continue our business operations in the normal course. Please view these and other risks described in the Company's filings with the Securities and Exchange Commission ("SEC"), including those identified in the "Risk Factors" section of the annual report on Form 10-K for the year ended December 31, 2021, and subsequent quarterly reports filed on Form 10-Q, as well as other filings it makes with the SEC. Any forward-looking statements in this stockholder letter represent the Company's views only as of the date of this release and should not be relied upon as representing its views as of any subsequent date. The Company specifically disclaims any obligation to update this information, as a result of future events or otherwise, except as required by applicable law.