February 25, 2021

Dear Shareholder:

We are happy to share the progress of Reven Holdings, Inc. ("Reven") for the 2020 year. Despite an unprecedented global pandemic, 2020 was another year filled with major milestones for the company. Our team persevered through an uncharted and rapidly changing regulatory landscape, and simultaneously worked diligently to move the company forward in preparation for Phase 2 Clinical Trials. We will share critical achievements broken down by operational areas and finish with a preview of expected goals for 2021. Although the year was full of unexpected challenges, many of them brought forth necessary changes within the company and market opportunities for us to pursue in what could have been a very financially detrimental year for us as a small under-capitalized company. Even though we raised half the funds of the previous year, we achieved significant clinical and nonclinical accomplishments surpassing any other single year we have been in operations. Much of that is directly attributable to a complete re-building of our clinical operations and development team led by the addition of our Chief Medical Officer and Chief Scientist, Dr. Fatih Uckun, MD, PhD. As difficult as it is to make difficult financial decisions and personnel changes, this past year required many of them for the long-term viability of the company and to achieve the milestones we needed to clinically. The executive team is proud to report that the results are positive. We achieved a far greater return on the investment dollars raised and spent in terms of creating a broader asset base and additional future revenue streams through clinical diversification into new therapeutic areas for RJX.

New Executive Hire Dr. Fatih Uckun, MD, PhD, Chief Medical Officer and Chief Scientific Officer

In July, the company hired Dr. Fatih Uckun as its Chief Medical Officer and Chief Scientific Officer. Dr. Uckun earned his doctoral degrees at University of Heidelberg in Germany and completed his residency training in Pediatrics, fellowship training in Hematology/Oncology/Blood and Bone Marrow Stem Cell Transplantation, as well as postdoctoral research training in immunology at the University of Minnesota. Dr. Uckun has more than 30 years of professional experience in developmental therapeutics and biopharmaceuticals. Dr. Uckun worked as a Professor of Therapeutic Radiology-Radiation Oncology, Pharmacology, and Pediatrics as well as Director of the Biotherapy Institute at the University of Minnesota (1986-1997), where he became the first recipient of the Endowed Hughes Chair in Biotherapy, and as a Professor of Pediatrics and Head of Translational Research in Leukemia and Lymphoma of the Children's Center for Cancer and Blood Diseases at the University of Southern California (2009-2015). From 2012-2015, Dr. Uckun served as chair of the Biotargeting Working Group and a Member of the Coordination and Governance Committee of the NCI Alliance for Nanotechnology in Cancer. Dr. Uckun also served senior clinical executive roles as Chief Medical Officer of Oncotelic and as Head of Immuno-Oncology at Ares Pharmaceuticals and Executive Medical Director and Strategy Lead in Global Oncology and Hematology at Syneos Health. Prior to this, he was Vice President of Research and Clinical Development at Nantkwest, Chief Scientific Officer of Jupiter Research Institute and, before

that, held senior-level scientific and research positions at Parker Hughes Institute and its cancer center, Paradigm Pharmaceuticals, and the Children's Cancer Study Group.

Just prior to joining Reven, Dr. Uckun was the in-house subject matter expert and head of a task force for COVID-19 related development projects for Worldwide Clinical Trials. While there, he was also responsible for bringing several multi-million-dollar development projects to the global contract research organization.

He has published more than 500 peer-reviewed papers and he has authored numerous review articles and book chapters and is an inventor on numerous patents. He received numerous awards including the Stohlman Memorial Award of the Leukemia Society of America (now known as the Leukemia and Lymphoma Society/LLS), the highest honor given to a Leukemia Society Scholar. Most recently, he was named the recipient of the 2018 Turkish Academy of Sciences/TUBA Academy Prize in Health and Life Science. He has served as a member of several editorial boards and NIH grant review/special emphasis panels.

New Executive Hire: Jeffrey Halverson, Chief Financial Officer

Mr. Halverson is known as an exceptional leader with effective management and team building skills. As an experienced banking executive, he has an impressive 30-plus year track record of opening and growing banking organizations, with an emphasis in management and business development for community banking.

In 2009, Halverson co-founded a privately held finance company with a focus on providing advisory services to federally regulated financial institutions across the United States. Since 2014, Halverson has served as the founder and Chief Executive Officer of American Sky Financial, a Commercial and Residential Mortgage company serving community banks and developers nationwide.

Halverson's involvement in charitable organizations includes previously held board positions for the Levitt Pavilion Foundation, Eagle Valley Family Assistance Fund, the Communications Board for the American Bankers Association, and Habitat for Humanity. He holds a degree in Business Administration from Moorhead State University.

New Staff Hires: Expertise in Clinical Development, Quality Assurance, Regulatory Affairs

Nancy Oelke – 25 yrs of drug development, GMP Quality Assurance and Regulatory Experience

Renae Townsend – 20 yrs Drug Development and Clinical Research

Cynthia Lee, PhD Biochemistry and Molecular Biology, Regulatory Affairs and Drug Development. Expertise in IND and NDA development with the FDA as well as orphan drug and rare pediatric disease requests.

Reven Awarded Second IND

On October 21, 2020 Reven was awarded the approval to proceed with their second Investigational New Drug (IND) application from the FDA and second Phase 2 human clinical trial. The IND provides Reven with an opportunity to treat COVID-19 patients with its RJX drug product. For more information on the second IND please click the link below:

https://reven.com/press-release/reven-pharmaceuticals-wins-fda-approval-of-its-ind-application-for-treatment-of-covid-19-with-rejuveinix-rjx/

Orphan Drug Applications

Reven submitted two Orphan Drug Applications in Q4. On September 28, 2020 we submitted an application for Multisystem Inflammatory Syndrome in Children (MIS-C) and on October 6, 2020 we submitted an application for Pediatric Crohn's Disease. We expect to receive a response from the agency in the coming months. At present, COVID-19 related initiatives are taking precedent with respect to resource allocation at the FDA.

Clinical Development/FDA

The FDA-approved randomized, double blind Phase 2 clinical trial of RJX in COVID-19 patients is underway at multiple clinical trials sites in Texas.

Four large US centers with high COVID-19 patient volumes have agreed to participate in the study. IRB approvals have been obtained and contracts have been negotiated and executed with each of the four centers. Several backup sites have been identified for unexpected contingencies. The firm commitment from these centers is anticipated to significantly accelerate the clinical development for Reven's COVID-19 project in addition to future planned clinical studies for new indications. All clinical site personnel and Reven personnel have completed their advanced training certification for compliance with Good Clinical Practices (GCP).

Drug Safety Monitoring Board (DSMB)

Reven has developed a formal DSMB to ensure the proper identification, evaluation and adjudication of any unexpected or serious adverse events as we move into the Phase 2 trial. This is an important safeguard as we advance to treating sick patients rather than healthy volunteers.

Data Management and Statistical Services

Reven has contracted with an expert firm in the data management and statistical analysis services aspects of clinical trials. This particular firm was chosen among several qualified candidates because of their exemplary attention to detail and quality. They also have some unique and proprietary methods to allow for the integration and analysis of multiple data sets where there is a common link – in our case the use of RJX for instance.

Please follow our upcoming studies progress at the link below:

https://www.clinicaltrials.gov/ct2/show/NCT04708340?term=RJX&draw=2&rank=1

Manufacturing

In February, Reven sign an agreement with a US-based pharmaceutical manufacturing company. This agreement gave Reven a partnership with a drug manufacturer that has scalable commercial production capabilities. In July, we completed our first GMP manufacturing run with the company. We are currently working on scale-up production with the new manufacturer to help us manufacture larger quantities of RJX in the future capable of supporting orders of the magnitude to fulfill government size requisitions.

Non-Clinical

Our Non-Clinical work included reaching 18 months of formal stability in June. This was a major milestone for the company as it provided RJX with 18 months of product stability. We look forward to achieving 30 months of stability in May 2021. We also tested and released RJX for our upcoming COVID-19 related study. The team completed an in-vitro genotoxicity required safety testing which demonstrated the RJX formulation is not prone to inducing genetic damage. A potency assay was established to evaluate antioxidant activity of RJX. The team also completed a 14-day comparative toxicity study between two slightly different formulations of RJX. Our Non-Clinical group finished a busy 2020 by conducting exploratory efficacy studies in rodent models for potential expanded indications.

Quality

Reven developed and implemented a new Quality program spanning all aspects of its clinical and nonclinical development projects. Reven's Quality team has been diligently working to keep the company compliant with the constantly changing regulations. In 2020, we completed 5 vendor audits and have three in progress. All Reven staff completed Good Clinical Practices (GCP) training. We also completed internal reviews and updates of all Standard Operating Procedures (SOPs) and training procedures.

Publications

Reven published five articles in 2020 and two in 2021. These articles introduce the safety of RJX and how it can potentially improve the outcomes in not only COVID-19, but also acute respiratory distress syndrome, sepsis, and other diseases that have heightened system inflammatory responses.

- Cabala K, Earabino J, Pacult P, Uckun FM. Rationale for a randomized, placebo-controlled, Phase 2 study of Rejuveinix (RJX) in COVID-19 patients with acute lung injury and hypoxemic respiratory failure. 2020;10:185-189. (https://www.openaccessjournals.com/articles/rationale-for-a-randomized-placebocontrolled-phase-2-study-of-rejuveinix-rjx-in-covid19-patients-with-acute-lung-injury-.pdf)
- Uckun FM, Carlson J, Orhan C, et al. Rejuveinix Shows a Favorable Clinical Safety Profile in Human Subjects and Exhibits Potent Preclinical Protective Activity in the Lipopolysaccharide-Galactosamine Mouse Model of Acute Respiratory Distress Syndrome and Multi-Organ Failure.

Front Pharmacol. 2020;11(November):1-18. doi:10.3389/fphar.2020.594321 (https://www.frontiersin.org/articles/10.3389/fphar.2020.594321/full)

- Uckun FM, Ervin J, Sahin K, et al. Clinical impact potential of Rejuveinix (RJX) for prevention of fatal acute respiratory distress syndrome (ARDS) and multi-organ failure in COVID-19 patients. 2020;10:177-184. (https://www.openaccessjournals.com/articles/clinical-impact-potential-of-rejuveinix-rjx-for-prevention-of-fatal-acute-respiratory-distress-syndrome-ards-and-multior.pdf)
- Ervin JD, Wyk H Van, Cabala K, et al. Rejuveinix (RJX) as a drug candidate for patients with systemic inflammatory response syndrome (SIRS): Supportive care considerations for COVID-19, cancer, and sepsis. Ann Pulm Crit Care Med. 2020;3(June):1-3. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7683794/pdf/fphar-11-594321.pdf)
- Uckun FM, Ozercan IH, Orhan C, Gitterle M, Sahin K. Rejuveinix Reverses Severe Inflammatory Lung Damage in a Mouse Model of Fatal Sepsis. 2021:1-8. doi: https://doi.org/10.1101/2020.12.31.424986 (https://www.biorxiv.org/content/10.1101/2020.12.31.424986v1)
- Uckun F, Orhan C, Powell J, et al. Non-clinical safety profile and pharmacodynamics of two formulations of the anti-sepsis drug candidate Rejuveinix. 2021:1-22. doi: doi.org/10.1101/2021.01.03.425139 (https://www.biorxiv.org/content/10.1101/2021.01.03.425139v1)
- Uckun F, Tuzcu M, Gitterle M, et al. Rejuveinix Mitigates Sepsis-Associated Oxidative Stress in the Brain of Mice Clinical Impact Potential in COVID-19 and Nervous System Disorders. bioRxiv. 2021:1-9. doi: https://doi.org/10.1101/2021.01.03.424883 (https://www.biorxiv.org/content/10.1101/2021.01.03.424883v1.full.pdf)

Sincerely,

The Reven Team