PROMETRIKA
A FULL-SERVICE CRO

NEWSLETTER

Message from the CEO

MIGANUSH STEPANIANS, PH.D.

Welcome to PROMETRIKA's 2020 year-end newsletter! This has truly been a remarkable year for us all. The global COVID-19 pandemic has had far reaching impact in a myriad of ways on how we live and work, and it continues to be the most consequential event of our times. The pandemic has given our industry a singular and unifying purpose and has shone a true positive light on our profession as developers of life saving treatments and vaccines. We are all thrilled to be a part of this industry and celebrate the great accomplishments achieved in a very short time against this deadly disease.

Throughout this eventful year, the PROMETRIKA team has continued its successful journey of providing high quality and flexible services to our community of more than 140 client companies. We are still working almost entirely remotely and are proud to have maintained seamless continuity of operations and delivery of service excellence. I am so grateful to our amazing employees who, through their hard work and adherence to high standards, have made PROMETRIKA better and stronger than ever this year.

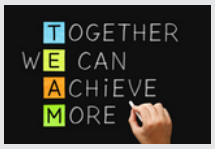
In 2020, our team has worked on more than 70 clinical trials, including several full-service trials. We have moved to production 6 databases and locked another 6. Our statisticians and programmers have analyzed the data for more than 50 studies, and our writers have collaborated on documents supporting 15 studies. As a team, we have collaborated on 6 NDAs, with one submitted to the FDA in 2020 and another 3 that will be submitted in 2021.

Our team is committed to a philosophy of continual improvement and strives each day to remain current with the latest technologies, methods, regulatory guidance, and our industry's collective approach to clinical research. I am thrilled that, today, all of our clinical and data management projects routinely and successfully leverage an array of technological tools for more efficient, flexible, and transparent study conduct, including advanced data analytics, eTMF, CTMS, targeted SDV, interactive web randomization and trial supply management, and imaging data repositories.

On behalf of the entire PROMETRIKA Team, I send you all my best wishes for a successful 2021. May the New Year bring advancements and greater success in development of new medicines to help improve the lives of patients and their families.

Kind regards,

Webinar Series



Keys to a Successful Rare Disease Natural History Study

In 2021, PROMETRIKA will be offering a series of upcoming webinars focused on rare disease natural history studies. As a full-service CRO, we have witnessed the challenges of designing a successful natural history study. Please join us to hear from our experts and fellow industry leaders about overcoming logistical, study design, and statistical challenges in rare diseases.

Forging Successful Sponsor-Academia Collaborations

- Models for collaboration and the unique challenges associated with a rare disease indication.
- Overcoming operational challenges.
- Adapting your natural history study strategy for rare diseases.

Practical Challenges in the Real World

- Unexpected challenges of designing natural history studies for rare diseases.
- How to adapt the study design within the evolving landscape of COVID-19.
- Designing a database that is fit-for-purpose, instead of a traditional EDC design.

A Statistical Problem at Its Core

- The different tools in the statistics arsenal for tackling data analysis in natural history studies in rare disease.
- Case studies from our expert biostatisticians with 20+ years of experience.
- What you might miss in your natural history data.

PROMETRIKA was happy to once again participate in the **Medidata NEXT Global 2020** conference. The breadth of discussion reflected Medidata's finger on the pulse of the clinical research landscape in these uncertain times. There was a strong emphasis on leveraging technology to maintain patient participation continuity in clinical trials and there were several tracks dedicated to the use of real world evidence for clinical trials in which data collection may currently be limited.

FEEDING AMERICA

Food insecurity is affecting many people in these trying times. PROMETRIKA strives to help and has recently completed a second round of donations to 12 food banks, located in the cities and states where our employees reside.

Lead and Impact: Turning Innovation Into Practice

Tommy Dossett, Senior Biostatistician, attended the virtual [ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop] in September 2020. Tommy attended a presentation on:

Causal Inference for Real-World Evidence: Propensity Score Methods and Case Study

Propensity scores represent the probability that a patient received treatment given various patient characteristics such as age and gender. In non-randomized studies, propensity scores are used to ensure that the distribution of observed baseline covariates are the same between treated and untreated subjects. Because propensity scores allow real-world data to be analyzed as if collected from a randomized clinical trial, causal inference can be made about the treatment for the population of interest.

Cancer Immunotherapy

Neil Wohlford, Principal Biostatistician, attended the virtual Symposium on the Role of Statistics in Cancer Immunotherapy. This year's symposium focused on how increased use of immunotherapies in cancer treatment over the past decade has changed how clinical trials in oncology must be designed and analyzed. Due to the delayed benefit often seen with immunotherapy agents, the standard methods generally used to estimate survival benefit in oncology trials are often not optimal for analyzing trials of immunotherapies.

The FDA has endorsed the use of analysis techniques that are more appropriate to immunotherapies. One such technique is restricted mean survival time (RMST). A major barrier, though, to designing trials using techniques like RMST is the lack of methods available to properly estimate the sample size.

MassBio Patient Advocacy Summit

Chelsey Ryan, Associate Director of Clinical Operations and Pharmacovigilance, recently attended **MassBio Patient Advocacy Summit**. The message at the summit was clear and consistent: incorporating the "voice of the patient" is a key component in the design of successful clinical trials. Recognizing patient needs and behaviors during protocol design can increase enrollment, reduce sponsor timelines and help ensure that the study's measures of efficacy include what is important to the patient (and thus to the drug's eventual consumers). Incorporating measures to increase patient compliance can also reduce sponsor cost.

Hearing directly from patients and the leaders of patient advocacy groups was inspiring and underscored the fundamental principle that guides our work: to positively impact the longevity and quality of life for the patients we serve.

PROMETRIKA AND SAAMA TECHNOLOGIES

Enhancing Remote Monitoring

PROMETRIKA's continuing partnership with Saama has streamlined our ability to provide robust real-time data analytics. Our high standards for data quality and trial design, paired with the powerful Saama analytical tools, enable us to provide real-time safety oversight and risk-based quality management of the clinical trials that we support. In the midst of the COVID-19 pandemic, this partnership has proven to be invaluable as we continue to integrate more remote and centralized monitoring offerings.

CONGRATULATIONS

Stoke Therapeutics has published two important articles related to their research in rare diseases. In Nature Communications, the company reports on their proprietary approach to addressing severe genetic diseases by precisely upregulating protein expression using Targeted Augmentation of Nuclear Gene Output (TANGO). In Science Translational Medicine, preclinical data from studies on STK-001 demonstrate significant improvements in survival and reductions in seizure frequency in a Dravet syndrome mouse model. In August 2020 the first human patient was dosed in a Phase 1/2a study of STK-001.

Lantheus Holdings [formerly Progenics Pharmacueticals] has submitted a new drug application (NDA) to the FDA for PyL™ (18F-DCFPyL), a prostate specific membrane antigen (PSMA)-targeted positron emission tomography (PET) imaging agent for prostate cancer. The NDA is supported by data from two pivotal studies (OSPREY and CONDOR), which examined the ability of PyL to reliably detect and localize disease. PyL will play an ongoing role in the diagnosis and management of prostate cancer.