RARE DISEASES NEWSLETTER
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WELCOME TO THE SEVENTH EDITION OF THE RARE DISEASES NEWSLETTER!

This quarterly publication will keep you up to date on PRA's rare disease team, experience, achievements, and initiatives.

EDITION HIGHLIGHTS

THE RARE DISEASE TEAM ANNOUNCES THE ADDITION OF 2 NEW CLINICAL SCIENTISTS: DEREK ANSEL AND AMY RAYMOND

DEREK ANSEL, CLINICAL SCIENTIST, RARE DISEASES, is a three-time US Pharma-Times Clinical Researcher of the Year finalist. He has 6 years of experience in clinical laboratory research, monitoring, and project management across trial Phases I-IV. He is currently completing his Master's degree in Pharmacology and Toxicology from Michigan State University. Derek has a wide breadth of experience in many therapeutic areas including vaccines, infectious diseases, and nephrology. In addition, his rare disease expertise includes pediatric pulmonary arterial hypertension, hemophilia A & B, von Willebrand disease, thrombotic thrombocytopenic purpura, and eosinophilic esophagitis. Excited by integrative technologies, Derek is well-versed in SAS programming and SharePoint development, and this expertise further enhances the collaborative efforts of his clinical teams. Outside of business hours, he is a writer for the Vaccine Education Center at the Children's Hospital of Philadelphia and an active consultant for several start-ups within the eClinical software space.

AMY RAYMOND, CLINICAL SCIENTIST, RARE DISEASES, has over 20 years of experience from all points of the pipeline: basic research, drug discovery, pre-clinical, and clinical research. She holds a bachelor's degree in molecular and cell biology from the University of Arizona, and earner her doctorate in molecular and cellular biology in the San Diego State/University of California San Diego joint doctoral program. Amy's extensive experience in public-private partnerships and collaborations have resulted in several publications, and she has presented these findings at many national and international conferences. In her career, Amy has been a meaningful contributor across a wide array of indications, from rare pediatric cancers to rare neurodegenerative disorders, such as amyotrophic lateral sclerosis and Huntington's disease. Amy is passionate about enhancing the efficiency of clinical trials to deliver much needed treatments through cooperative productivity and data-driven, patient-centered design. In her spare time, she is very active in her local chapters of SoCRA and ACRP, helping raise the profile of clinical research, expand the talent pool of qualified clinical researchers, and engages with the community on continuing clinical research education.

DISEASE SPOTLIGHT:

X-LINKED ADRENOLEUKODYSTROPHY

X-linked adrenoleukodystrophy (X-ALD) is the most common peroxisomal disorder that affects 1 in 18 000 people. It most severely affects boys and men. The disease is caused by mutations in the ABCD1 gene that encodes the peroxisomal membrane protein ALDP which is involved in the transmembrane transport of very long-chain fatty acids (VLCFA; ≥C22). A defect in ALDP results in elevated levels of VLCFA in plasma and tissues. It mainly affects the nervous system and the adrenal glands, which are small glands located on top of each kidney. In this disorder, the fatty covering (myelin) that insulates nerves in the brain and spinal cord is prone to deterioration (demyelination), which reduces the ability of the nerves to relay information to the brain. In addition, damage to the outer layer of the adrenal glands (adrenal cortex) causes a shortage of certain hormones (adrenocortical insufficiency). Adrenocortical insufficiency may cause weakness, weight loss, skin changes, vomiting, and coma.

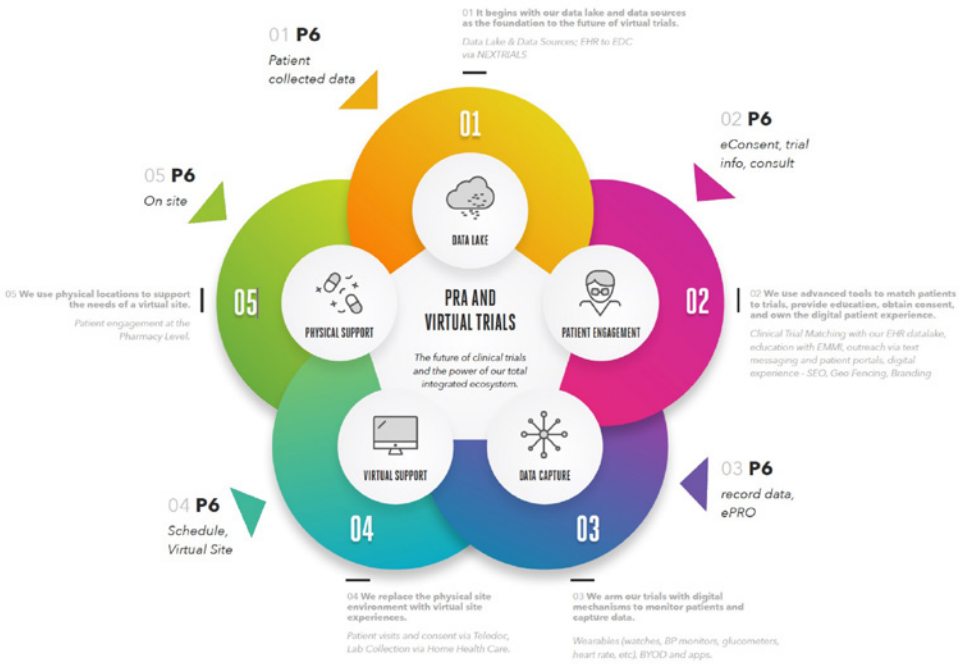
There are three distinct types of X-ALD: a childhood cerebral form, an adrenomyeloneuropathy type, and a form referred to as Addison disease. The childhood cerebral form is the most common form of ALD, representing about 45% of all ALD cases. It is characterized by an inflammatory process that destroys the myelin, causing relentless progressive deterioration to a vegetative state or death, usually within five years. The majority of other cases of the disease occur as the adult form, known as adrenomyeloneuropathy type. Beginning in their 20s and 30s, these young men exhibit neurological based motor lesions in their extremities. These lesions progress over many years and are inevitably accompanied by moderate to severe handicap. The progress of the disease is slower, usually declining to a vegetative state and/or death in 5 years or longer. Patients with X-ALD whose only symptom is adrenocortical insufficiency are said to have the Addison disease form.

Disease Spotlight: X-linked adrenoleukodystrophy continued

For patients with Addison disease, adrenocortical insufficiency can begin anytime between childhood and adulthood. For the majority of patients with X-ALD there is currently no curative or preventive treatment. In boys and adolescents with early-stage cerebral ALD, allogeneic hematopoietic stem cell transplantation (HSCT) can arrest the progression of cerebral demyelination in ALD provided the procedure is performed at a very early stage of the disease. However, several promising new approaches will hopefully come to fruition in the future. For example, it has been demonstrated in X-ALD cells that small interfering RNA (siRNA)-mediated inhibition of ELOVL fatty acid elongase 1 (ELOVL1) reduces VLCFA synthesis and levels. Compounds that can inhibit ELOVL1 are therefore interesting candidates for new preventive treatments. It is anticipated that in the not too distant future transplantation of autologous hematopoietic cells that have been genetically corrected with a lentiviral vector prior to re-infusion might become an additional therapeutic option. The Starbeam Study (ALD-102) is a Phase 2/3 investigational gene therapy study to determine the safety and tolerability of Lenti-D while determining if the one-time treatment can stop the progression of cerebral ALD. PRA's significant corporate experience gives us an understanding of the specific nuances of running these studies including ensuring quality data, endpoint selection and leveraging our relationships with the multiple stakeholders such as KOLs and patient advocacy groups.

END-TO-END RARE DISEASE STUDY PLATFORM - PARALLEL6: CLINICAL6 PLATFORM

CLINICAL6 provides an end-to-end, patient-centric mobile Clinical platform for patient enrollment, engagement and management. While these modules can benefit many trials, the platform enables solutions to major hurdles that are quite common in the rare disease space. Clinical6 supports enrollment with eConsent and study websites, portals, and apps and dashboards that are customized for the CRO, PI & site perspectives. Engagement is accomplished through both a patient engagement module, as well as the Care Circle module, recognizing the invaluable contribution to rare disease patient care partners. Engagement tools used for faster data collection and compliance are: eDiaries, ePRO, EDC, symptom reporting, scheduling and more. Protocol compliance and the patient experience will both enhanced by the CLINICAL6 telemedicine module, which supports virtual patient encounters with audio and video chat capabilities. PRA's exclusive partnership with Intel's Care Innovations allows the Clinical6 platform to extend beyond the palm of the patient or care circle of stakeholders, but into the home with connected devices and wearables. The rare disease team has already begun incorporating this technology in study proposals, and looks forward to lowering the barriers and supporting success of rare disease clinical trials by incorporating the CLINICAL6 platform.



RARE DISEASE INDICATIONS WE ARE ACTIVELY PURSUING:

- Hereditary Hemochromatosis
- Spinal Muscular Atrophy
- Amyotrophic Lateral Sclerosis
- Prader Willi Syndrome
- Fragile X Syndrome
- Primary Immune Deficiency
- Paroxysmal Nocturnal Hemoglobinuria
- Atypical Hemolytic Uremic Syndrome
- Retinitis Pigmentosa
- All muscular dystrophies

THIRD QUARTER HIGHLIGHTS

NEWLY AWARDED RARE DISEASE STUDIES:

- Beta Thalassemia – Ph 2 Study
- Hemolytic Disease of Fetus and Newborn – PoC study & LTFU Registry
- X- Linked Hyposphapatemia – Disease Monitoring Program
- Sly Syndrome – Disease Monitoring Program
- Myasthenia Gravis – Ph 2 study
- Duchenne Muscular Dystrophy – Ph 2 study
- Phenylketonuria syndrome – Ph 1 study
- Spinal Muscular Atrophy – Ph 2 study

WHERE WE'VE BEEN

- Rare Disease Team at Global Genes 2017 RARE Patient Advocacy Summit, 14-15 September 2017, Irvine, CA
- Scott and Lisa, joined by Business Development and Marketing, attended and presented at the DIA meeting in Chicago.
- Lisa attended the Cure SMA Surf Day with Ricochet The SURFice dog

WHERE YOU CAN FIND US NEXT

- Scott and Derek at "Disorder – Rare Disease Film Festival", 02-03 October 2017, Boston, MA
- Scott presenting "Overcoming the Challenges of Conducting Clinical Studies in Rare Pediatric Populations" with Mark Sorrentino, xTalks, 11 October 2017 (http://xtalks.com/Clinical-Studies-in-Rare-Pediatric-Populations.html)
- Sravan at SOCRA Annual Conference, 06-08 October 2017, Orlando, FL
- Scott at NORD Annual Rare Disease Summit 16-17 October 2017, Washington DC
- Scott and Lisa at World Orphan Drug Congress, 13-15 November 2017, Barcelona, Spain

CONTACT INFO

If you need assistance with a rare disease study, have a particular personal interest in rare diseases, or would like more information, please contact us at:

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DRIVING INSIGHT TO ACTION (DIA) 2017

The Driving Insights to Action (DIA) Global Annual Meeting took place June 19-21, 2017 in Chicago, IL. Scott Schliebner and Lisa Dilworth, from PRA's Rare Disease team, alongside many PRA colleagues attended the event. PRA team members attended the conference to deliver this key message: Fueled by technology, driven by insight, we help our clients deliver hope to patients. Scott Schliebner chaired a dynamic session titled "Engagement, Education, Networks, Media and Societies in Rare Diseases: The MUST Haves". Lisa Dilworth presented her abstract and Spinal Muscular Atrophy case study, "Integrating the Patient's Voice Across the Development Program of Rare Diseases: Translation into Meaningful Outcomes". In addition to these educational discussions, PRA had a vibrant presence at the exhibition booth, as well as at our sponsored client event at The Crown, in Tribune Tower.

CLICK ON THE LINKS BELOW TO ACCESS THE RECENTLY PUBLISHED WHITE PAPERS, BLOGS AND WEBCASTS FROM THE RARE DISEASE TEAM:

Whitepapers

Strategies for Accelerating Rare Disease Clinical Development

Multi-Stakeholder Collaborations Can Minimize Barriers & Drive Rare Disease Clinical Programs to Better Patient Outcomes

The Patient Voice: Engaging Rare Disease Patients Improves Clinical Trial Enrollment & Retention

Blogs

https://prahs.com/blog/2017/07/17/rare-diseases-and-the-promise-of-gene-therapy-what-you-need-to-know/

https://prahs.com/blog/2017/08/07/finding-a-cure-for-spinal-muscular-atrophy/

https://prahs.com/blog/2017/06/12/a-mother-inspires-as-she-battles-rare-disease/

Webcasts

The Patient Voice - Engaging Rare Disease Patients to Accelerate Clinical Trial Enrollment

Strategies and Collaborations to Accelerate Rare Disease Clinical Development