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Conference Proceedings

The Epilepsy Foundation's 4th Biennial Epilepsy Pipeline Update Conference

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ABSTRACT

On June 5 and 6, 2014, the Epilepsy Foundation held its 4th Biennial Epilepsy Pipeline Update Conference, an initiative of the Epilepsy Therapy Project, which showcased the most promising epilepsy innovations from health-care companies and academic laboratories dedicated to pioneering and advancing drugs, biologics, technologies, devices, and diagnostics for epilepsy. Speakers and attendees included emerging biotech and medical technology companies, major pharmaceutical and device companies, as well as investigators and innovators at the cutting-edge of epilepsy. The program included panel discussions on collaboration between small and large companies, how to get products in need of funding to the marketplace, who is currently funding epilepsy and CNS innovation, and how the NIH facilitates early-stage drug development. Finally, the conference featured the third annual "Shark Tank" competition. The presentations are summarized in this paper, which is followed by a compilation of the meeting poster abstracts.

1. Introduction

On June 5 and 6, 2014, the Epilepsy Foundation (EF), based in Landover, Maryland, USA, held its 4th Biennial Epilepsy Pipeline Update Conference, an initiative of the Epilepsy Therapy Project, at the Hyatt Regency in San Francisco, California. Showcasing the most promising epilepsy therapies from health-care companies and academic laboratories dedicated to pioneering and advancing drugs, biologics, technologies, and devices for epilepsy, this conference also featured the third annual "Shark Tank" competition. On the day following the Pipeline conference, a day-long program was held for people with epilepsy, families, and advocates.

The Epilepsy Pipeline Update Conference brought together decision-makers with shared interests in epilepsy treatment and diagnosis and product development. Speakers and attendees included emerging biotech and medical technology companies, major pharmaceutical and device companies, as well as investigators and innovators at the cutting-edge of epilepsy and advances in treatment of central nervous system (CNS) diseases.

The program also included panel discussions on topics such as the role of collaboration between small and large companies, how to get products in need of funding to the marketplace, who is funding epilepsy and CNS innovation today, and how the NIH facilitates early-stage drug development.

"The Epilepsy Foundation's Pipeline Conference is recognized as the premier business and scientific forum for driving innovation in the field of epilepsy and neurology," said Philip M. Gattone, President and CEO of the Epilepsy Foundation. "Each year, this conference brings together great minds in R&D, clinical thought leaders, investors, and industry leaders who are focused on accelerating epilepsy drug and device development."

"This conference has grown to attract an impressive audience. Companies are recognizing the need for and promise in developing potential new therapeutics for epilepsy," said Jacqueline French, MD, Professor of Neurology, New York University.

The "Shark Tank" competition, held on the second day of the conference, is designed to spur breakthroughs that will change the lives of people living with epilepsy. Over the past two years, entrepreneurs, scientists, clinicians, industrial design engineers, and members of the epilepsy community have been recognized for their truly inventive product concepts, which have ranged from promising new therapeutics or technologies to new products that improve the quality of life for people living with epilepsy. At the 2014 Epilepsy Pipeline Conference, the

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winner was selected by live audience vote from the epilepsy community and a panel of distinguished reviewers. The Shark Tank award recipients received international recognition and cash prizes totaling $200,000 to fund the development of novel ideas.

The authors of this report attended the conference and wrote the text based on hearing the presentations at the conference as well as reviewing the meeting recordings (http://www.epilepsy.com/information/professionals/epilepsy-foundation-events-webcasts), which are recommended to readers interested in more details as well as the question-and-answer sessions. Most but not all of the presentation summaries were reviewed for accuracy by speakers. The affiliations and titles of authors are accurate as of the date of their presentation, but may have since changed.

2. Session 1: introduction and keynote address

2.1. Introduction. Philip Gattone, President and Chief Executive Officer, Epilepsy Foundation; Warren Lammert, Chairman, Board of Directors, Epilepsy Foundation

Mr. Phillip Gattone, CEO and President of EF, opened the conference. Mr. Gattone remarked that this Pipeline Conference is the first to be webcast (http://www.epilepsy.com/information/professionals/epilepsy-foundation-events-webcasts) and streamed live over Epilepsy.com. He welcomed all participants and stressed the importance of this conference, which helps to uniquely unify the epilepsy community with active participation from patient advocates, venture capitalists, basic scientists, pharmaceutical and device industry companies, and clinicians. Mr. Gattone then introduced Mr. Warren Lammert, Chairman of the Epilepsy Foundation Board of Directors. Mr. Lammert also welcomed all participants to this unique conference and highlighted how this conference furthers the vision of the Epilepsy Foundation research mission in order to help bolster the translation of novel ideas into new treatments for patients with epilepsy in an expedited manner.

2.2. The annual state of the drug pipeline — keynote. Jacqueline French, MD, Professor of Neurology, New York University; Co-director, Epilepsy Research and Epilepsy Clinical Trials, NYU Comprehensive Epilepsy Center; President, Epilepsy Study Consortium

Dr. French highlighted the fact that although there are many treatments that have become available for epilepsy, there is still a paucity of treatment for those who have drug-resistant epilepsy and for numerous epilepsy syndromes. In particular, she pointed out that a better way to predict the effectiveness of various drugs is needed. There are still too few options for newly diagnosed patients as many of the advances in epilepsy management are directed to those with drug-resistant epilepsy. In addition, there is a paucity of treatments for the comorbidities of epilepsy. Even more importantly, there are no therapies that truly prevent the disease. Most treatments are geared towards the concept of preventing further seizures but we do not have any antiepileptogenic or disease-modifying therapies. Even when a drug is approved, neither animal models nor clinical trials predict if a drug will be successful in day-to-day clinical practice. Despite many new approved antiepileptic drugs (AEDs), there are few in phase II trials [1]. Dr. French summarized her presentation by reminding the audience that so much more work is needed to discover new AEDs with the ability to truly help patients.

2.3. Annual state of the device pipeline — keynote. Robert Fisher, MD, PhD, Maslah Saul Professor of Neurology, Director, Stanford Comprehensive Epilepsy Program

Dr. Fisher divided his comments into different categories of devices. Specifically, he discussed seizure alerts or predictors; adherence monitors; clinical information systems; optical control or optogenetics; new ways of drug delivery; focal energy such as radiosurgery, laser, and ultrasound; and neurostimulation.

Regarding seizure alerts, SmartWatch and EpiAlert are currently available. These devices alert caregivers of seizures via wireless mobile phones or PDAs. Novel systems that alert patients and caregivers to their seizures are being devised. These systems operate on seizure detection by electrodermal responses, muscle activity by electromyography, or electroencephalography (EEG) patches [2–4]. For seizure prediction, a device is in trials in which implantable EEG leads are placed in the area of a seizure focus which attach to a personal advisory device that alerts patients when a seizure is likely to occur [5].

Adherence monitors are compliance-alerting devices with the ability to instantly provide information about pill-taking, blood test readouts of AED levels, or even when a pill reaches the stomach. Related to compliance devices are seizure diaries with three currently available online epilepsy diaries: My Epilepsy Diary, Seizuretracker.com, and Patients Like Me.

These diary applications help to better provide information to health-care practitioners and to the patients themselves as self-management tools.

Optogenetics is a promising technique where light-induced signals can either excite or inhibit neuronal activity, carrying with it the promise of enhancing epilepsy management. One of the provided examples was the idea of using a yellow light that activates a rhodopsin gene, which in turn opens a chloride channel, hyperpolarizing a transfected neuron and rapidly stopping the neuron from firing [6].

There are a number of therapeutic devices with the ability to deliver treatment by novel approaches including inhalation, buccal absorption, and infusion pumps. Focal energy can also be delivered to ablate epileptic tissue, such as with stereotactic radiosurgery or thermal ablation [7]. Focused ultrasound is a very new potential treatment with some promise. Lastly, various neuromodulatory techniques, including vagus nerve stimulation, transcranial magnetic brain stimulation, trigeminal nerve stimulation, thalamic deep brain stimulation, and responsive neurostimulation, are either currently available or being trialed [8,9].

3. Session 2: what was better in 2013 than 2012 — progress in epilepsy therapy

3.1. FDA and epilepsy trials: past, present, and future. Russell Katz, MD, Consultant, Epilepsy Study Consortium

Dr. Russell Katz, consultant to the Epilepsy Study Consortium and former Food and Drug Administration (FDA) official, discussed the FDA and epilepsy trials: past, present, and future. He noted that in particular, there are four areas in which the FDA is considering new forms of acceptable data: monotherapy indication, pediatric indication, design of add-on trials, and controlled released products.

Monotherapy claims are difficult to attain because of the ethical concerns about performing trials where standard of care is withdrawn for the drug being studied, and further, it has been difficult to extrapolate information from add-on trials. He pointed out problems with not accepting equivalence trials, yet companies want to have a monotherapy claim. A white paper has been drafted, and the FDA is reviewing it in order to address these issues and look for novel ways to approve a monotherapy indication, including possibly extrapolating from add-on studies, if proper dosing information is available.

Pediatric claims have always required that a clinical trial be performed in pediatric patients. However, pediatric claims based on adult clinical trials can be made, assuming the disease is similar in both the adults and children in a sufficient manner that one could make that claim in a reliable and safe manner, and that pediatric dosing could be provided. However, to date, these criteria have not been considered to have been met. Therefore, the FDA is working on finding novel ways to establish those claims, including the possibility that extrapolation from adult data might be acceptable.