5TH ANNUAL WORLD ORPHAN DRUG CONGRESS

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WELCOME

The category of orphan drugs has become a focal point of enormous weight and significance in the healthcare industry. As the category continues to flourish, the learning curve has been steep and challenging for all those involved in bringing these drugs to market.

The World Orphan Drug Congress represents an ideal forum for pharma, payers, regulators, and patient advocacy groups to exchange ideas on sustainability, pricing and reimbursement, commercialization, and global market access. This confluence of perspectives has resulted in remarkable learnings, deeply rooted in compassionate insights that transcend economic concerns, elevating the importance—and urgency—of improving patients' lives.

This collective mindset is reflective of an industry working together to accelerate the process of marketing breakthrough treatments to people suffering with rare diseases—an historically abandoned group in desperate need of medical help once thought impossible to achieve. This labyrinth of connectivity reflects a collaborative spirit, encouraging the community's constituents to fully capitalize on an immense collective brain trust: Generating awareness and engagement; fearlessly defining and achieving goals; improving treatment options; optimizing adherence and therapeutic benefit; establishing trusted lines of communication and freedom from judgment.

This report captures our observations and key learnings from attending the 5th Annual World Orphan Drug Congress in the United States.

Enclosed you will find high-level summaries from core presentations, concentrating on science, research, and development; patient groups and advocacy; and considerations around access, reimbursement, and the regulatory landscape.

JUICE remains committed to helping you keep current with new findings and developments in the rare disease space, and we hope that you will find the enclosed information useful.

Enjoy,

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EXECUTIVE SUMMARY

The conference featured rich content distributed across a range of formats—round-tables, presentations, and podium discussions explored clinical development, patient partnerships, regulatory approval, reimbursement, global trends, manufacturing, distribution, orphan drug business models, and commercialization strategies.

Alongside the main conference track, which hosted the moderators and speakers, the Congress offered a number of corresponding tracks to maximize opportunities for industry executives, middle managers, scientists, and end users to interact with and learn from one another:

- Roundtable sessions
  These intimate sessions brought constituents together at the same table who were mutually interested in the products and services of other participants.

- Pitch & Partner sessions
  Early-stage orphan drug development and in-licensing/commercializing orphan drugs in late stage or in the market require partnerships and capital. These sessions provided the fertile ground needed for interested parties to meet one another.

- Seminar theater presentations
  Small biotechs and other entrants in the rare disease space had an opportunity to present their case studies, and to educate and inform a highly relevant target audience of potential customers or partners of their specific programs.

- Pre-conference workshops
  How to establish market potential for an investor audience and how to find common ground in patient advocacy engagement and collaboration were the 2 key-issue workshops to hone in on in the rare disease space.

- Exhibition showcase floor
  The exhibitor space provided ample opportunity for sponsors to build presence for their brands and raise the profile of their companies and organizations.

SESSIONS REVIEW

Keynotes and Great Debates: Assisting the diagnoses of rare diseases with facial recognition software, and drawing a picture of the future sustainability in the orphan drug space

Christoffer Nellaker, Research Fellow at the Medical Research Foundation's Functional Genomics Unit, Oxford University, demonstrated in his keynote how clinically relevant metric features extracted from ordinary photographs could help inform the diagnostic process in rare diseases—roughly one third of the 7,000+ rare diseases have some kind of craniofacial manifestation. Facial recognition software identifies rare diseases based on algorithmically determined phenotypes. This completely automatic system produces consistent predictions; it is adaptive and accounts for variations in ethnicity, age, and gender. In summary, this type of technology can use readily available photos and narrows the search space for syndrome diagnosis.

In his video keynote, Henri Termeer, Former Chairman, President, and CEO of Genzyme, discussed aspects of sustainability in the orphan space. Main aspects revolved around how market and industry will change over the next 5 to 10 years, and how one can prepare to face the challenges. He brought some thought provoking what-if ideas, such as "Will orphan drugs get capped at a certain amount, ie, at $500K per patient per year?" or "Are payers just exaggerating the quantitative burden of rare disease patients in order to argue that the total cost would be unaffordable?" In summary, Termeer believes that there will be better finance solutions in the future, and they will be dependent on investments that still need to be made. He said: "The future is extremely bright and the best example is this meeting right now, bringing people all in the same area to network."

Stephanie Okey, Genzyme's SVP and Head of North America, Genetic Diseases, and US General Manager, made a case in her presentation for good medicine being good business by meeting unmet needs in an effort to transform lives. During her presentation, she touched upon issues such as sustaining the rare disease business, taking into consideration the payers' perspective; developing medicines for and with the patients as a focal point; and articulating the clinical value of orphan drugs. Sustainable care in the rare disease business is one of the key concerns in the United States, and close partnerships are one way to attain this goal.

In the Great Debate "The Price Is Too Damn High! …or Is It?" Ed Pezalla from Aetna was concerned with whether there will be continued access to medication. He pointed out that money spent on healthcare cannot be spent anywhere else. Jeff Myers of Medicaid Health Plans of America added that, as a market, healthcare is somewhat of an anomaly because its prices aren't necessarily determined by supply and demand in the way traditional markets function. This often leads to reactions such as "We can't afford it." On the other side of the debate, Douglas Paul, PharmD, PhD, Vice President and Partner, Medical Marketing Economics, LLC, argued that as the rare disease population is so small the rest of the population can more than cover the cost. The prices of orphan drugs indeed *are* what makes this sector sustainable and attractive: The high costs are necessary for innovation, and the question the debate boils down to is, "Are we going to fund innovation or not?"

The panelists were each given 1 minute to come up with a solution for their sides. There were mentions of better planning steps, for instance, to take advantage of discounted drug prices when available; and suggestions to have the development of drugs to come with some sort of equity that can be owned by a manufacturer; and finally that drug companies should take more risks in drug development just like every other segment in healthcare.

Launching the first therapy for Duchenne muscular dystrophy (DMD) after a 16-year journey

Mark Rothera, Chief Commercial Officer of PTC Therapeutics, spoke about launching ataluren, the first therapy for nonsense mutation Duchenne muscular dystrophy (nmDMD) after a strenuous 16-year journey, and about the collaboration with the expert community and international patient groups from research to development to commercialization. DMD is a recessive X-linked form of muscular dystrophy, resulting in muscle degeneration and premature death. The disorder is caused by a mutation in the dystrophin gene, compromising a protein that provides structural stability to the muscle-cell membrane.

In his presentation, Rothera touched upon the pros and cons of partnering for launch and discussed the importance of early and expanded access programs: Access for Translarna™ (ataluren) is expanding rapidly, focusing first on fastest-access geographic areas. Currently not yet approved in the United States, Translarna received conditional approval in the EU in August 2014.

PTC Therapeutics has persevered through unchartered territory in drug discovery, clinical development, and commercialization for the first drug approved to treat nmDMD. Translarna is a "read-though medication" for nonsense mutations—about 2,000 monogenetic diseases are caused by nonsense mutations that cause read-through issues: As a precision medicine for a rare disorder, Translarna has the potential for broad application. To ensure that in its current indication, Translarna is delivered to the right patients, PTC is tackling the issues, which include late diagnosis, lack of knowledge of genotype, lack of genetic testing, and the patients' often significant distance to major diagnostic and treatment centers.

Kate Holland, VP, Sales and Marketing, Vanda Pharmaceuticals, spoke about the intricacies of the unmet needs surrounding a rare, severe circadian rhythm disorder called non-24-hour sleep-wake disorder. It almost exclusively occurs in people who suffer from total blindness, sometimes also termed NLP (no light perception) blindness. The pineal gland's unawareness of the daytime in those patients results in an inability to physiologically adjust the circadian clock based on light perception, thus causing a shift in sleep/wake rhythm, excruciating drowsiness and fatigue during the day, and insomnia during the night.

Holland talked about the grassroots method of achieving expanded disease awareness and commercial success without a patient group. Some of the points touched upon included how traditional marketing early in the process can help raise awareness for a rare disease; how patients can be empowered to actively seek "patient-directed physician visits"; and how knowledge gaps and incorrect diagnoses can be overcome.

Building the cures of the future—FDA's programs to boost orphan drug development

Richard Moscicki, MD, Deputy Center Director for Science Operations, Center for Drug Evaluation and Research, FDA, discussed programs to advance orphan drug development in his presentation about building the cures of the future. These include, for instance, the FDA's tools to expand rare disease treatments, from vouchers to incentives, and expanding means of communication with pharmaceutical companies. Moscicki shared some interesting numbers with the audience, for example, that 41 new orphan drugs have been approved in the past year, 41% of which were first-in-class. Since the FDA Safety and Innovation Act of 2012, 86 new therapies have been designated as "breakthrough therapies" by the FDA's Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER).

Value-based or cost-based pricing? Where are we headed as a society that needs to be able to afford its healthcare?

Julie Stoss, Vice President, Government Relations at Kaiser Permanente, provides strategic counseling as a legislative support representative in Washington, DC, and her presentation was an open and honest discussion about pricing, and about the value and sustainability of pricing in orphan drugs. With her example of the first generation of direct-acting hepatitis C treatments, she made the question of value in new breakthrough drugs tangible. Patients described their experience with those treatments like the "worst flu in your life," and a staggering 25% did not get cured of their chronic infection. Now, with the second-generation hepatitis C drugs, and a near 100% cure rate with virtually no side effects, there's no debate to be had about value. But the dispute revolves around price, and with that, about the fear that in no way costs that high can be sustainable over time.

In Stoss' words, gone are the days for all of us where cost, profit, and margin could dictate price—today price has to be looked at in the context of government, resources, families, and tax payers: 17% of the GDP goes toward medical expenses—and the government is not limiting pricing, not negotiating, not getting involved at all in an effort to preserve and protect a model that, as could be heard in other presentations at WODC this year, accounts for 95% of all new treatments and therapies being developed in the United States. It is designed to create incentives, awards, innovation, and additional benefits for Orphan drugs because they're at a disadvantage to begin with. Those were the intentions behind the Orphan drug Act of 1983, and its unintended consequences today are that developing orphan drugs is no longer intrinsically disadvantaged but priced at ranges to create enormous profits.

Stoss admittedly picked extreme examples that would for argument's sake support her point; she wanted to encourage stakeholders to navigate wisely, to "not overshock the market," pointing out that as a society, "we cannot afford a blank check." Her provocative line returned to its origin, to the question of how to determine value. She chose measles to illuminate the gap between value-based and cost-based pricing. If value-based, we'd be spending $3.5B on measles, and eradication of polio would have never been possible if it was priced based on value, not cost. Stoss suggested that for any drug over $10K per patient per year, it should be required to disclose information such as development cost to have a better discussion of "What should the price be?"

EXHIBITION SHOWCASE FLOOR

The exhibition floor was the central hub for connecting rare disease specialists with each other and it showcased the latest in patient registries, consultancy/specialty pharma/legal services, and technology, just to name a few.

The exhibition floor was a great place to meet and mingle, and to generate new business leads. Exhibitors enjoyed building presence for their brands, raising the profile of their companies and organizations. There was ample opportunity to forge strategic partnerships and joint ventures, as well as to showcase the latest products and innovations to prospective buyers, and to promote new services, educating the target market on the latest service offerings.

At this year's World Orphan Drug Congress, in collaboration with Terrapinn, the organizers of the event, we were able to continue our opportunity sponsoring the Congress with a JUICE Pharma Worldwide booth. Together with Malcolm MacKenzie, SVP, Strategic Planning and Customer Insights, Alec Pollak, VP, Director of User Experience, and Isaac Epstein, New Business Coordinator, we were able to share important and relevant case studies on how JUICE has dealt with challenges in launching and marketing orphan drugs.

Views of the exhibitor floor and the JUICE booth with Isaac Epstein and Malcolm MacKenzie.