ADVANCED THERAPIES IN THE CNS:
TIME TO GET SMART

Moderator: Joel Sandler, PhD, Assoc. Principal, Defined Health
Panelists: Steven Gray, PhD, Assoc. Professor, UT Southwestern
Mike Rice, MS, MBA, Principal, Defined Health

Advanced Therapeutics Webinar
16 October, 2018
Advanced Therapies Trajectory – Hype Cycle With a (Positive) Twist

The Biotech Death of Jesse Gelsinger

ExCLUSIVE: First gene therapy drug sets million-euro price record

Value and Count of "Gene Therapy" Licensing Deals

AveXis Enters Agreement to be Acquired by Novartis AG for $8.7 billion
- Novartis to acquire AveXis for $218 per share in cash
- AveXis’ lead product candidate, AVXS-101, expected to enhance Novartis’s position as a gene therapy and neuroscience leader
- Transaction expected to be completed in mid-2018

Chicago, April 09, 2018 (GLOBE NEWSWIRE) – AveXis, Inc. (NASDAQ:AVXS)

FDA approves novel gene therapy to treat patients with a rare form of inherited vision loss
Luxturna is the first gene therapy approved in the U.S. to target a disease caused by mutations in a specific gene

Sciencenews
November 26, 2014, 12:40 PM

Annual Count of "Gene Therapy" Pubmed Publications

Visibility

Maturity
Recent Defined Health Advanced Therapies Webinar* Highlighted Areas Where Gene Therapy is Poised to Disrupt Pharma Franchises

♦ Example: Hemophilia
  • Current treatment costs >$250K/yr per patient, requiring IV infusions every 2 weeks
  • Gene Therapy could provide lifelong treatment after one IV dose.

♦ Example: IEMs
  • ERT costs $200-500K/yr per patient, requiring regular IV infusions. Often not curative, patients still need extensive supportive care.
  • Gene Therapy could provide lifelong treatment after one dose.

While Oncology Players Can *Probably* Safely Sit on the Sidelines and Wait for Data, Inactivity in Gene Therapy By Ophthalmology, Hemophilia and IEM Companies May Carry Threat of Therapeutic Franchise Obsolescence

Recent Defined Health Advanced Therapies Webinar* Highlighted Areas Where Gene Therapy is Poised to Disrupt Pharma Franchises (CNS DISORDERS NOT MENTIONED)

Beyond MS, migraine, and certain psychiatry markets, there are no franchises to supplant

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CNS Disorders
- Proteinopathies
- Epilepsies
- Genetic disorders

Ophthalmology
- Allergan
- Novartis
- Regeneron

Hemophilia
- CSL
- Novo Nordisk
- Grifols
- Shire
- Bioverativ

Inborn Errors of Metabolism (IEM)
- Sanofi
- Biogen

CNS Advanced Therapies Market Does Not For Lack for...

...Unmet Need
Majority of Genetic Disorders Have a Central or Peripheral Neurological Component

- Genetic involvement in the pathogenesis of neurological disease is significant
- Genetic disorders affect the central and peripheral nervous system
- Among the approximately 6,400 phenotypic entries in cataloged inherited human diseases:
  - Central nervous system disorders account for ~60%
  - Peripheral nervous system disorders for ~15%.
- Can be broadly categorized as
  - Hereditary Myopathies
  - Neuropathies
  - Epilepsies
  - Neuromuscular
  - Movement disorders (Ataxias and spasticity)
  - Sensory Disorders (ophthalmologic, otologic)

~60% of the entries in Defined Health’s Genetic Disease Database are believed to have neurological involvement

CNS Advanced Therapies Market Does Not For Lack for... ...White Space

Of the Estimated 3,000 Genetic Diseases with a Neurological Component, Only ~10% Have an Identifiable Therapeutic Candidate in Development

*List includes lead indications for all viral gene therapy products in preclinical or clinical stages of development for each of the four buckets indicated (sensory, metabolism/endocrinology [non-CNS indications deleted], musculoskeletal [pure osteo indications deleted], and neurology) as identified from pipeline databases (Adis, Cortellis) and subsequently annotated by Defined Health.
CNS Advanced Therapies Market Does Not For lack for...

...Partnering/M&A/Investor Activity

**06/06/2018**

Oxford BioMedica and Axovant Sciences enter into a $842.5 Million Exclusive Worldwide Licence Agreement for OXB-102 for the Treatment of Parkinson’s Disease

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**09/10/2018**

Sangamo and Pfizer Announce Collaboration for Development of Zinc Finger Protein Gene Therapy for ALS

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**02/20/2019**

AbbVie and Voyager Announce Global Strategic Collaboration to Develop Potential New Treatments for Alzheimer’s Disease and Other Tau-Related Neurodegenerative Disorders

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**09/10/2018**

PTC Therapeutics to Acquire Agilis Biotherapeutics

- Expands and diversifies current pipeline with four gene therapy programs
- BLA submission in AADC deficiency expected in 2021

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**07/19/2018**

Novartis enters agreement to acquire AveXis Inc. for USD 8.7bn to transform care in SMA and expand position as a gene therapy and Neuroscience leader

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**06/26/2018**

Takeda commits to a $230M package to seal blockbuster neurological R&D deal with Wave Life Sciences

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**02/20/2018**

VENTURE FUNDING OF US THERAPEUTIC COMPANIES BY DISEASE, 2016 VS. 2017

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**02/20/2018**

GLOBAL LICENSING OF R&D-STAGE THERAPEUTICS BY DISEASE, 2016 VS. 2017

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**02/20/2018**

CNS Advanced Therapies Market Does Not For Lack for...

...Regulatory Incentives

- Early Alzheimer’s Disease: Developing Drugs for Treatment Guidance for Industry
- Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment Guidance for Industry
- Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment Guidance for Industry
- Rare Pediatric Disease Priority Review Voucher Program
- Human Gene Therapy for Rare Diseases Draft Guidance for Industry
- Expedited Programs for Regenerative Medicine Therapies for Serious Conditions Draft Guidance for Industry

FDA.gov
Elements Collectively Appear to be Lining Up for Broad Value Inflection
Advanced Therapies Trajectory – Hype Cycle With a (Positive) Twist?

Where the cycle goes next will be determined by clinical performance but also sound strategic decision-making (positioning, partnering, pricing), which must be supported by an awareness of both technical and commercial considerations.
An Overnight Success (that Took Decades to Transpire): Commercial Success Contingent on Technical Aptitude (and Vice Versa)

Disease mechanism (mono- vs. polygenic, cell autonomy, dominance, tissue)?

Vehicle (tropism, packaging constraints, distribution)?

Modality (knockdown vs. edit vs. augment, persistence)?

Dosing (timing, bioavailability, invasiveness, volume)?

Host immunity (autoimmune reactions vs. vector, gene product, target tissue)?

Translational risk?

Clinical-regulatory path?

Positioning, sustainability (brands, portfolios)?

Market exclusivity vs. trade secrets, iteration?

Manufacturing, scalability?

Market access hurdles?

Cost-effectiveness

Bioethics issues?
Advanced Therapies in the CNS: Time to Get Smart
The Panel

TECHNICAL QUESTIONS

BUSINESS MODEL QUESTIONS

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Questions for My Panelists

TECHNICAL QUESTIONS

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