Gene Therapies for Rare Central Nervous System Genetic Disorders: A Landscape

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BACKGROUND

- As of today, there are over 7000 rare diseases identified[1] and estimated to be nearly 30 million people in Europe and 25 million in North America who suffer from a rare disease.[2]
- Central Nervous System (CNS) diseases are expected to reach 14.7% of the global disease burden by 2020, making it the largest burden of any disease group, thus, the demand for CNS therapies will be expected to increase.[3]
- Rare diseases possess unique and inherent challenges in terms of traditional development, market access, and reimbursement processes and frameworks.
- The complexity and burden of CNS diseases, especially rare CNS diseases, in conjunction with the complexity of gene therapy, provide a platform on which much insight is to gain.
- Zolgensma®, a gene therapy treating Spinal Muscular Atrophy, is the first gene therapy targeting a rare CNS disease to reach the market in the United States.
- Currently, several gene therapies, targeting various rare CNS diseases, are in development.
- With large unmet needs, an increasing burden in rare CNS diseases, and limited literature available, a landscape of gene therapies for rare CNS diseases is merited.

OBJECTIVE

- A landscape of gene therapies for rare CNS diseases in clinical trials provides a deeper understanding of the rare CNS disease field, eventually allowing for the anticipation of rare CNS disease gene therapies reaching the market and their challenges in development, evaluation, and pricing and reimbursement.
- The landscape will identify the number of diseases with current gene therapy clinical trial information available, the status of their clinical trials, the phases in which they currently are, and the entity funding these gene therapy clinical trials for rare CNS diseases, among other critical data.

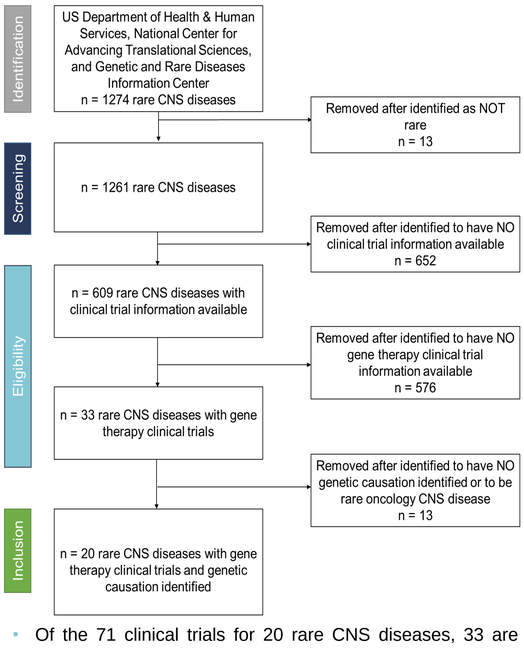
METHODOLOGY

- A systematic review of rare CNS disease gene therapy clinical trials was conducted using the U.S. Department of Health and Human Services[4], National Center for Advancing Translational Sciences[5], Genetic and Rare Diseases Information Center[6], and the U.S. National Library of Medicine Clinical Trials[7] databases.
- The rare CNS disease gene therapy clinical trial data extracted included disease name, condition, NCT number, title of trial, acronym of trial, status, study results, intervention, outcome measures, sponsor/collaborators, gender, age, phases, enrollment, funded by, study type, study designs, other IDs, start date, primary completion date, completion date, first posted, results first posted, last update posted, locations, and study documents.
- An initial analysis of gene therapy clinical trials for rare CNS diseases was conducted.

RESULTS

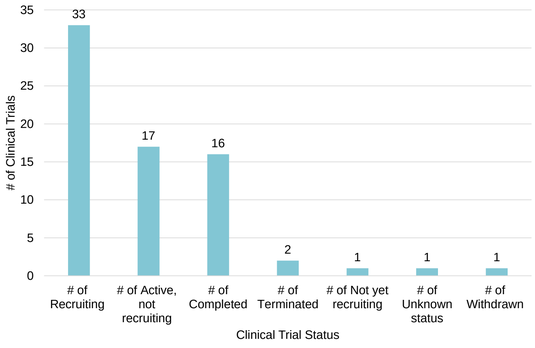
- Of the 1274 rare CNS diseases identified, 20 rare CNS diseases with identified genetic causation had gene therapy clinical trial data, with 71 clinical trials identified.

Figure 1. Systematic Review of Gene Therapy Clinical Trials for rare CNS diseases Flow Chart



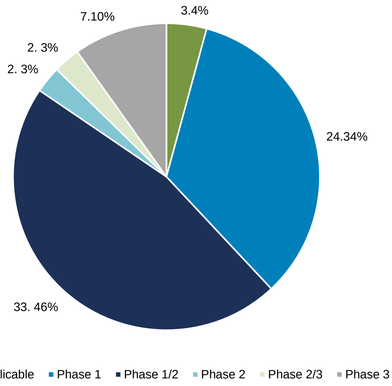
- Of the 71 clinical trials for 20 rare CNS diseases, 33 are currently recruiting, 17 are active and not recruiting, 16 are completed, 2 have been terminated, 1 is not yet recruiting, 1 has been withdrawn, and 1 has an unknown status.
- The majority of the clinical trials identified for gene therapy in rare CNS diseases are recruiting (Figure 2).

Figure 2. Clinical Trial Status of Rare CNS Gene Therapy Clinical Trials



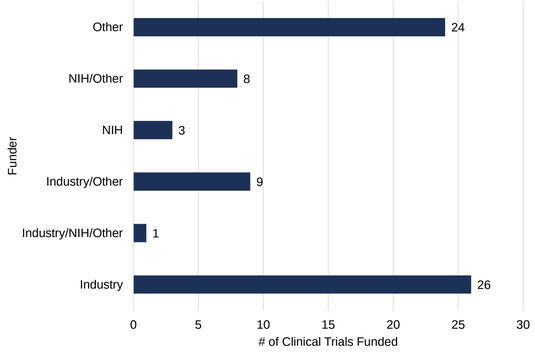
- The majority of the clinical trials identified for gene therapy in rare CNS diseases are in Phase 1/2 (Figure 3):
  - Of the 71 clinical trials for 20 rare CNS diseases: 33.46% are in Phase 1/2, 24.34% are in Phase 1, 7.10% are in Phase 3, 2.3% are in Phase 2, and 2.3% are in Phase 2/3, while 3.4% have “not applicable” phase status assigned to them.

Figure 3. Clinical Trial Phase for Rare CNS Gene Therapy Clinical Trials



- The majority of the clinical trials identified for gene therapy in rare CNS diseases are funded by Industry (Figure 4):
  - Of the 71 clinical trials for 20 rare CNS diseases: 26 are funded by Industry, 24 are funded by Other, 9 by Industry/Other, 8 by NIH (National Institutes of Health)/Other, 3 by NIH, and 1 by Industry/NIH/Other.

Figure 4. Clinical Trial Funding for Rare CNS Diseases Gene Therapies



CONCLUSIONS

Of the 1274 rare CNS diseases, less than 2% have gene therapy clinical trial information available. As identified in this landscape, the majority of gene therapy clinical trials are recruiting (47%) and in phase 1/2 (33%) for rare CNS diseases, and the majority of these trials are being funded by the Industry (37%) as well as other entities (34%). With limited available literature on rare CNS disease gene therapies, the field merits further investigation to anticipate and address the unique challenges of their impending arrival in current, traditional market access frameworks.

REFERENCES
1. Richter, Trevor, Sandra Nestler-Parr, Robert Babela, Zeba M. Khan, Theresa Tesoro, Elizabeth Molsen, and Dyfrig A. Hughes. "Rare Disease Terminology and Definitions—A Systematic Global Review: Report of the ISPOR Rare Disease Special Interest Group." Value in Health 18, no. 6 (2015): 906-14. doi:10.1016/j.jval.2015.05.008.
2. Schieppati, Arrigo, Jan-Inge Henter, Erica Daina, and Anita Aperia. "Why Rare Diseases Are an Important Medical and Social Issue."
3. "Better Days Ahead? The Emerging State of CNS Drug Development." Premier Research. May 17, 2018.
4. https://www.hhs.gov/
5. https://ncats.nih.gov/
6. https://rarediseases.info.nih.gov/diseases/diseases-by-category/17/nervous-system-diseases
7. https://clinicaltrials.gov/

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