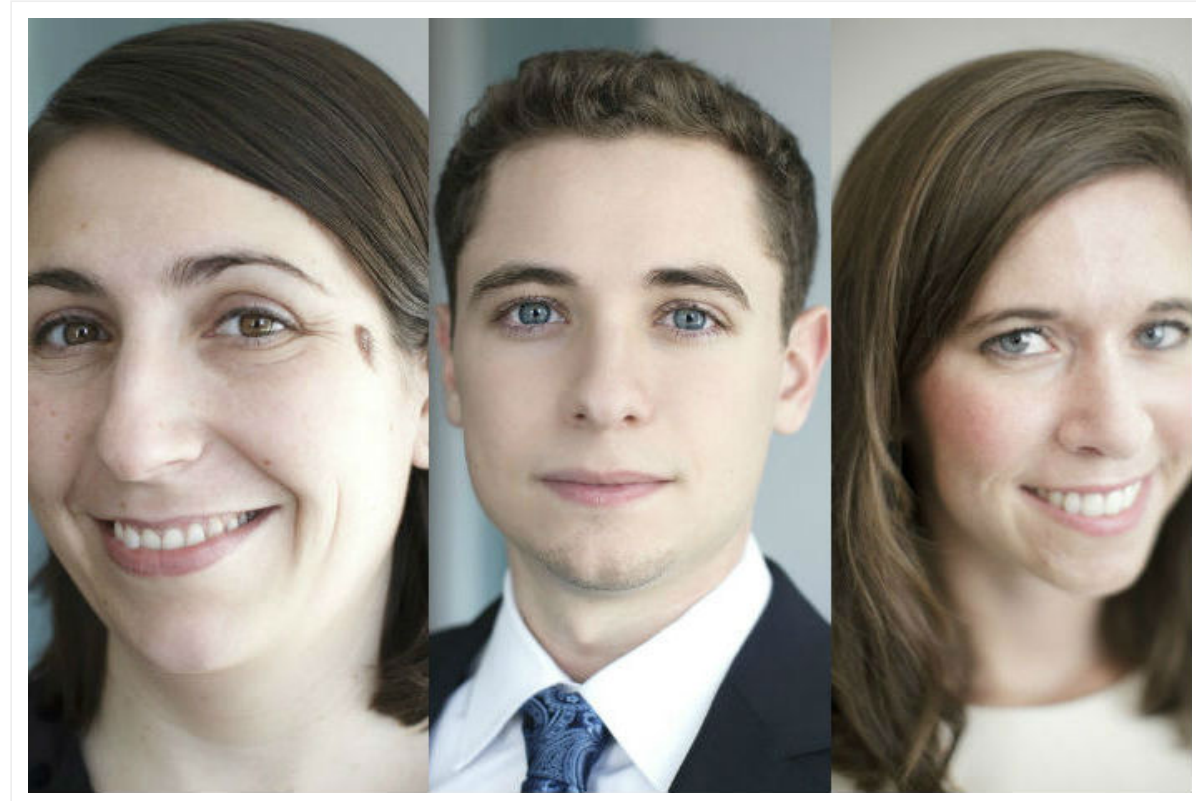


SMA therapy: paving the way for drug development strategies



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Alessia Deglincerti (pictured above, left), Frank Borowsky and Rachel Laing from consulting firm Bionest Partners, explore in an Expert View how the development of spinal muscular atrophy (SMA) therapies could provide a blueprint for genetic diseases.

Disease-modifying therapeutics have vigorously entered the market for the treatment of SMA, a rare sight for neurological and neuromuscular diseases.

The development of these SMA drugs not only brings new opportunities for additional, supportive drugs as a new SMA disease progression emerges, but also provides companies with a blueprint for franchise, commercial, and payer strategies that can be translated to other diseases where next-generation therapies will also become the new standard of care.

A newly-evolving disease

Gene therapies such as those approved to treat SMA are making a major impact in the field of medicine.

These treatments are designed to address the genetic problem underlying a disease and thus help reduce the severity of the condition while potentially increasing lifespan considerably. For example, infants diagnosed with the most aggressive form of SMA, Type 1, have classically been unable to move by six months old and in need of ventilation and feeding tubes by the age of two.

Survival would not go beyond a few years of age. Treatment with new disease-modifying agents, however, is leveling out disease progression, enabling patients to walk and breathe on their own, past the typical lifespan of the disease.

While these therapies have demonstrated efficacy, it still remains unclear as to how these drugs will alter the natural course of the disease. It is uncertain how long these therapies will sustain their effects and in which patient populations they will be most effective. We are entering uncharted territory in SMA: patients may experience residual, and possibly new symptoms that will need to be managed as part of a new definition of the disease.

Focusing the development of new drug candidates

This “new” disease course gives companies the opportunity to develop novel therapies with various mechanisms of actions and targets, including supportive therapies that can work in combination with the disease-modifying medicines.

Understanding the new disease course is an important area for drug developers. Companies developing new drugs in the space will need to follow upcoming, longitudinal studies and deep dive into real-world evidence from treated patients to understand the disease course and identify remaining unmet needs.

By doing so, we may well start to define various patient sub-groups, each with different disease progression, symptoms, and unmet needs. This information can then be used by companies to develop therapies specifically targeted for these sub-populations.

Next, companies need to decide the most appropriate clinical endpoints and milestones to achieve.

These measurements, which are vital in determining payer reimbursement for outcomes-based models, will be best addressed by evaluating how the new course of the disease presents itself, and may require new assessment tools that have so far not been explored in the condition.

Additionally, companies also need to consider the possibility of combination therapies for SMA and how payers will address those costs when multiple drugs are utilized.

To achieve these goals and inform the clinical development strategy, it is critical that companies consult with patients, advocates, disease experts, regulators, and health technology assessment groups early on during the drug development process.

Extrapolating to other diseases

SMA has been a first example demonstrating how disease-modifying agents that enter the clinic are not only shifting the patients' medical needs but also influencing further clinical development and implementation of new treatments.

Companies can use the history of SMA, which is a disease that affects a small population, and extrapolate this experience to hundreds of other rare genetic diseases. Gene-modifying technologies have advanced significantly over the past few years, as companies have worked through some early challenges, including scalability, accurate cell targeting and innate immune responses.

As the industry develops platforms that can be translated for use across multiple indications, we can expect to see similar efforts in other ultra-rare genetic diseases that would benefit from gene-modifying therapy.

Learnings from the SMA story will be extrapolated to other diseases, making it a blueprint for development and market access.

At the same time, companies focused on providing supportive therapies in other genetic conditions can look at the evolution of the SMA franchises in an effort to remain competitive in their respective fields even as disease-modifying drugs reach the market.

Additionally, many neuromuscular and neurodegenerative disorders such as multiple sclerosis, Alzheimer's disease and Duchenne Muscular Dystrophy (DMD) carry common symptoms. By focusing on symptomatic treatments, companies have the opportunity to develop therapies that cover a wide range of indications.

New SMA therapies are also good examples of drugs that have achieved favorable reimbursement decisions from payers through an outcomes-based model. For drug developers, this can act as a model of cost-effectiveness and evidence-based development, which needs to be closely evaluated.

Taken together, the evolution of SMA therapies has paved the way for the development of other disease-modifying agents, which could potentially become the standard for genetic diseases, even beyond neurological and neuromuscular conditions. Companies developing drugs in these other fields are uniquely positioned to use SMA as a case study and enrich their development, commercial, and market access strategies.

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