The pace of therapy development in SMA is unprecedented, given that the causative gene was only discovered in 1995.

It’s a hopeful time for SMA patients and families, as promising therapies are moving closer to approval.

- The gene that causes the majority of SMA cases has been identified (*survival motor neuron gene 1; SMN1*).
- The clinical presentation and disease course for SMA are well understood.
- We can largely predict the severity of disease based upon how many copies patients have of the *SMN1* backup gene (called *SMN2*).
- A rich history of research focusing on the biology of motor neurons (the nerve cells that die in SMA), including innovative ways to study these cells in a dish, informs today’s studies.
- Reliable animal models for studying SMA have been created.
- Exciting therapies targeting the genetic cause of SMA have been developed and are currently being tested in humans. These include drug, antisense and gene therapy approaches, all of which act by increasing the amount of SMN protein.

### 20 Years of Progress for SMA

Ten years ago, we had just two potential drugs in the beginning stages of preclinical discovery. Five years ago, we had four. Today we have almost 20, including seven now in clinical trials.
Although exciting therapies are in the pipeline for SMA, much remains to be done to expand our basic knowledge of the disease and ensure patients have safe and effective treatment options.

### The second wave of SMA therapies

Experimental therapies for SMA currently are being tested, but it’s unknown how effective they will be. We must improve upon first-generation approaches, as well as augment them, utilizing a combination approach with other strategies under development such as those designed to maximize muscle contraction.

#### MDA action

We are funding the development of antisense therapies that target parts of the SMN gene not targeted by therapies currently in clinical trials. The hope is that we can capitalize on the knowledge already generated and maximize this approach to raise SMN levels in patients. Additionally, MDA-funded researchers are testing combinatorial therapies as a synergistic strategy for SMA. For example, one of our scientists is combining antisense therapy with three different types of approaches to target the nerves, supporting cells, and muscle.

### Newborn screening

It’s widely thought that earlier treatment will lead to better outcomes in people with SMA. Currently, SMA is not screened for at birth; however, addition of SMA to the newborn screening panel could help in the early identification and treatment of patients.

#### MDA action

MDA has long been committed to newborn screening efforts and is involved in the policymaking aspects of newborn screening at the federal level. MDA has valuable experience in newborn screening and will leverage that knowledge in promoting newborn screening for SMA and other muscle debilitating diseases.

### Improved prediction of disease severity

Disease severity is predicted based largely on the number of patient copies of the SMN1 backup gene (called SMN2). However, this copy number does not always correlate with disease severity. Especially as therapies near the approval stage and options become available, we need to give families accurate predictions for disease severity so that they can weigh the risks and benefits of therapeutic interventions.

#### MDA action

MDA is funding world-renowned geneticists to examine how other “modifier” genes in addition to SMN2 differ from patient to patient, and how these differences may affect and help predict disease course. We are also supporting a nationwide-network of biomarker studies to develop improved measures to follow disease progression that will aid in determining whether therapies in trials are effective or not.

### Motor neuron biology

Decades have been devoted to understanding the function of motor neurons. However, research into how these cells develop and communicate with other cells continues to provide insight into what goes awry in SMA and other diseases.

#### MDA action

MDA takes a big-picture perspective across SMA and related neuromuscular diseases to uncover breakthroughs that will accelerate treatments and cures. The power in this “umbrella” approach is that knowledge and information from one disease can often yield progress in others. We can take what we’ve learned about motor neurons in ALS, for example, and apply these lessons to SMA. In addition to numerous other studies, we are currently funding exciting work studying how the SMN protein gets trafficked down long motor neurons as well as how motor neurons controlling breathing differ from other motor neuron subtypes.

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