Neurological disorders are a group of more than 1,000 conditions that affect the brain and nervous system. Together, these disorders impact an estimated 100 million Americans, nearly a third of the U.S. population. Although some are well known, such as epilepsy, migraine headaches, multiple sclerosis and Parkinson’s disease, many are rare, affecting just a small number of patients. Of the more than 7,000 known rare diseases, about 360 of them are primarily neurological, including amyotrophic lateral sclerosis (ALS) and Huntington’s disease.

According to a recent study, the cost and incidence of neurological disorders is expected to increase as the number of Americans ages 65 and over is projected to nearly double, from 43.1 million in 2011 to 83.7 million in 2050. Because neurological disorders are more prevalent in older adults and people are living longer (as a result of decreases in the number of deaths from cardiovascular disease and cancer), there is an unprecedented increase in the number of people affected by neurological disorders. With these numbers on the rise, it is more important than ever that new treatments that both modify disease and prevent disease are found.

Today, biopharmaceutical research companies are developing 537 medicines for numerous, wide-ranging neurological disorders. There is hope on the horizon, as scientists are uncovering more about how the nervous system works at the molecular and genetic levels, driving the development of innovative treatments for several neurological disorders. A recent report found that 74 percent of medicines in the biopharmaceutical pipeline for neurological disorders are potentially “first-in-class.”

The 537 medicines in development include:

- 95 medicines for brain tumors, including gliomas, which represent nearly 25 percent of all primary brain tumors. Nearly 80,000 new cases of primary brain tumors are diagnosed each year.

- 92 medicines for Alzheimer’s disease and other dementias. Alzheimer’s affects about 5.5 million Americans, while other forms of dementia affect an additional 2.2 million people.
• 76 medicines for chronic pain and chronic pain conditions, which affect more than 25 million Americans.6 Chronic pain is defined as some form of pain every day for three months. It can take many forms, such as low back pain, cancer pain, joint pain and nerve pain and can be associated with an initial injury, an unknown cause or a chronic pain condition such as fibromyalgia, diabetic neuropathy or endometriosis.7

• 46 medicines for Parkinson's disease, which affects as many as one million Americans. This is a disorder that mainly targets the dopamine-producing neurons in the brain, causing tremors, balance issues and cognitive changes. Incidence of the disease is expected to nearly double by 2030.8,9

• 36 medicines for epilepsy and other seizure disorders. Epilepsy affects about 3.4 million Americans and is the fourth most common neurological disorder.10

• 34 medicines for neurological genetic disorders, including Rett syndrome, a rare neurodevelopmental disorder affecting brain development; and spinal muscular atrophy, a rare disease affecting the motor nerve cells in the spinal cord. Both disorders are caused by a gene defect and affect about one in 10,000 children.11 Other neurological medicines in development target brain injuries, Huntington's disease, muscular dystrophy, spasticity, spinal cord injury and Tourette's syndrome, among others. A list of neurological medicines in development can be viewed here.

Medicines in Development for Neurological Disorders

Many of the 537 medicines in development represent a growing understanding of the underlying mechanisms of neurological disorders. This enhanced understanding creates scientific progress over time and allows researchers to explore new pathways and scientific approaches to treat these complex disorders. Examples of innovative treatments in development include:

• A monoclonal antibody in development for the prevention of migraine headaches that binds to and inhibits the activity of calcitonin gene-related peptide (CGRP). CGRP is expressed in the nervous system, where it plays a role in controlling the dilation of blood vessels and the transmission of neuropathic pain signals. Research suggests that CGRP pathways may be involved in the development of migraines. Anti-CGRP antibodies are thought to help inhibit the transmission of pain signals associated with migraines.

• Several medicines in development for Alzheimer's disease are disease-modifying treatments that may stop or slow down disease progression by targeting one or more of the changes in the brain associated with the disease. These targets include beta-amyloid plaques that appear between nerve cells, tau protein tangles that damage and kill brain cells and a receptor that decreases a neurotransmitter necessary for the brain to think and function normally.

• Agitation (verbal or physical outbursts, general emotional distress, restlessness, pacing and shredding paper or tissues) associated with Alzheimer's disease affects nearly 50 percent of people diagnosed with the disease.12 A medicine approved for schizophrenia and major depressive disorder is also in development for agitation in Alzheimer's disease. The medicine modulates the activity of serotonin and dopamine receptors in the brain, which may decrease the agitation and restlessness associated with Alzheimer's disease.

• A monoclonal antibody in development for relapsing multiple sclerosis targets leucine rich repeat and immunoglobulin-like domain-containing protein 1 (LINGO1), a protein that is involved in the repair of myelin, a protective sheath covering the nerve fibers. In multiple sclerosis, the body's immune system attacks myelin. Damage to myelin disrupts communication among cells throughout the nervous system, impairing mobility, vision and thinking. LINGO1 may inhibit the cells in the brain that are involved in myelin repair and, by blocking LINGO1's production, the medicine could support the growth of myelin and restore nerve communication in multiple sclerosis patients.
• A monoclonal antibody in development for Huntington’s disease binds to and blocks the activity of Semaphorin 4D (SEMA4D), a protein that plays a key role in the neuroinflammatory processes that can cause inflammation in the brains of individuals with the disease. By blocking the activity of SEMA4D, it may slow or prevent the neurodegeneration in Huntington’s disease, a fatal disorder that causes the breakdown of nerve cells in the brain.

• A cell therapy in clinical trials for amyotrophic lateral sclerosis (ALS) uses transplanted mesenchymal stromal cells (MSCs), which are stem cells derived from the patient’s own bone marrow. The MSCs are then enriched outside the body and re-transplanted into the patient. MSCs are potent cells that can differentiate into a variety of cells, such as bone cells, muscle cells or fat cells. In this case, the cells have been customized to treat neurodegenerative diseases by secreting a variety of neurotrophic factors. Neurotrophic factors are known to support the survival of neurons in a variety of conditions, including neurodegenerative diseases, such as ALS.

• Antibody-drug conjugates (ADC) utilize a monoclonal antibody to deliver a chemotherapy drug to cancer cells, releasing the drug once in contact with the cancer cells. One ADC in development specifically targets epidermal growth factor receptors (EGFR), a growth factor that stimulates the proliferation of cell growth. This approach has the potential to provide more targeted therapy to the cancer and thus limit side effects. The medicine is being tested in patients with EGFR-amplified glioblastoma. EGFR amplification and overexpression are features of glioblastoma, with about 40 percent of glioblastomas overexpressing EGFR.  

What’s next from America’s biopharmaceutical research companies?

Biopharmaceutical innovation is resulting in a rapid pace of medical breakthroughs and scientific advancements. America’s biopharmaceutical companies are working diligently to uncover new targets, treatments and ultimately cures for diseases that impact patients’ lives.

Despite this steady stream of progress, there is still much left to learn about one of the most important unmet needs in medicine – neurological diseases. Alzheimer’s, multiple sclerosis and other diseases and disorders of the brain affect one in six people around the world, driving a demand for innovative solutions to complex illnesses. In order to fully understand how America’s biopharmaceutical research companies are tackling these complex diseases, we spoke to company research experts in the field of neurological health.
How is your company working to unlock the biology of these diseases and overcome research hurdles?

“AbbVie recently invested in a new research laboratory – The Foundational Neuroscience Center in Cambridge, Massachusetts – that is focused entirely on unlocking the science driving neurodegeneration and fostering the discovery of new therapies. This Center has been an ideal location to attract exceptional scientific talent and to establish collaborative relationships with some of the local leaders in the field.”

— James B. Summers, Ph.D., Vice President, Neuroscience Discovery Research, AbbVie

“We’re exploring new types of drugs for epilepsy that target refractory seizures and patient subpopulations where there is a tremendous unmet medical need. We’re also targeting pathologies that are common across a number of neurological disorders with targeted therapies that have the potential to change the course of a disease. The fact is there is no one answer for every patient, so we’re continually working to connect the right treatment at the right time to the right patient to help transform the lives of people living with severe diseases.”

— Jeff Wren, Executive Vice President and Head of Neurology Patient Value Unit, UCB

“Otsuka has a passion and commitment to continually challenge the understanding, design and delivery of treatments for neurological conditions. Our legacy of more than 20-years in this area shapes our knowledge that there is no one-size-fits-all solution to patient care. We push ourselves to think differently, seek out diverse collaborators and always put the patient first as we develop advanced treatments.”

— Raymond Sanchez, A.B., M.D., Senior Vice President, Global Clinical Development, CNS, Otsuka

What are you most excited about for the future of neurological disorder treatment?

“Advances in understanding the biology – including genetics – of rare neurological diseases are resulting in novel treatment approaches. Our aim is to translate these innovative approaches aligned with new biological knowledge to make a significant impact on these devastating diseases.”

— Gerard Marek, M.D., Executive Medical Director, Immunology, Infectious Disease, Transplant, CNS and Pain, Astellas

“I’m most excited by the promise of using new technologies such as machine learning and digital patient assessment to advance our understanding of these incredibly complex disorders. The potential of using new research tools such as optogenetics, brain mapping and a myriad of different potential biomarkers is extremely promising.”

— Michael Sand, Ph.D., M.P.H., Senior Clinical Program Leader, CNS, Clinical Development & Medical Affairs, Boehringer Ingelheim Pharmaceuticals

“While there have been significant advances and new clinical breakthroughs in multiple sclerosis, the burden continues to be high as it remains the leading cause of non-traumatic disability among young and middle-aged adults and there is still no cure. To that end, we recognize there is still much more to be done. We are looking to uncover new pathways within the immune system to better understand multiple sclerosis and seek to develop more tailored approaches to treating the disease that hopefully may bring us one step closer to a cure.”

— John Walsh, M.D., Vice President, Neurology & Immunology, U.S. Medical Affairs, EMD Serono

“Increasingly, we’re seeing that the successful companies in our business are those that can drive breakthrough innovations for patients. That’s our mission at Lilly, and that means we’ll have to address more novel biology. It will also probably mean smaller trials in early development looking for big signals. If we don’t see those big signals, we’ll move on. When we do see signs of a game-changer, that’s when we’ll go all-in because we know it could be a great medicine for patients.”

— Dan Skovronsky, M.D., Ph.D., Senior Vice President, Clinical and Product Development at Eli Lilly and Company
“Just as cancer has progressed from being a death sentence to often being treatable and in some cases curable, the next few decades will see far more effective treatments for a variety of neurological diseases. The exploration of how the immune system can influence brain diseases like Alzheimer’s is one of the more exciting new areas of research for us. We are currently investigating how an imbalance in the immune system can drive a permanent and unhealthy inflammation of the brain. Understanding the role of immune and neuronal interactions in brain disorders will hopefully point us toward new avenues to develop breakthrough treatments for patients.”

— Doug Williamson, M.D., Chief Medical Officer, Vice President U.S. Drug Development, Lundbeck

“Many neurological diseases that were previously intractable can now be attacked thanks to major advances in science. New preclinical modeling capabilities and the revolution in DNA sequencing are helping to guide many of our efforts to identify new therapeutic targets. This is an amazing time to be involved in neuroscience research as we strive to discover impactful medicines that will help patients suffering from neurological diseases.”

— Ricardo Dolmetsch, Global Head, Neuroscience Research, Novartis

How are you engaging in partnerships and collaborations to advance new treatments forward?

“We are open to collaborating with all stakeholders – patients, academia, industry and governments. Each group offers us incredible learning opportunities, and we know that in order to make advances, we need everyone’s perspectives and help. This reality of need for inclusiveness has caused an acceleration and increase in span of collaborations, where we now see them operating from bench-side to bedside. There has also been a diversification of types of collaborations. Our companies cover the gamut from early, basic science collaborations with academia at our J-Labs incubators that host burgeoning companies to public-private collaborations and consortia all over the world. We further engage in all of these exciting possible areas of collaboration through the Johnson & Johnson Innovation Centers and our external affairs activities and business development. All this work is tightly integrated with our scientific goals which are focused on great unmet patient needs and the promise of emerging potentially transformative science.”

— Luc Truyen, M.D., Ph.D., Global Head, Development and External Affairs, Neuroscience, Janssen Research & Development, LLC

“Our approach is to form truly collaborative partnerships with academia, biotech companies and pharmaceutical companies with drug discovery programs that either complement our internal pipeline of programs, or that can deliver the next generation of innovative therapies to patients. We are also interested in accessing late-stage and on-market assets in our priority disease areas, through either partnerships or acquisition, that may support a high unmet patient need and that meet our threshold for innovation.”

— Michael Maurer, Vice President, Neuroscience Therapeutic Area Commercial Leader, Takeda
Public-Private Partnership to Tackle Alzheimer’s Disease and Parkinson’s Disease

The National Institutes of Health (NIH) has joined forces with biopharmaceutical research companies and non-profit organizations to accelerate the development of effective new treatments for Alzheimer’s disease and Parkinson’s disease. The initiatives are part of NIH’s broader Accelerating Medicines Partnership (AMP) – a public-private partnership between the NIH, the U.S. Food and Drug Administration (FDA), biopharmaceutical and life science companies, and non-profit organizations focused on transforming how new diagnostics and treatments are developed by jointly identifying and validating promising biological targets for therapeutics. In addition to Alzheimer’s and Parkinson’s, AMP is focused on type 2 diabetes, rheumatoid arthritis and lupus.

According to the NIH, prevalence of both Alzheimer’s disease and Parkinson’s disease are expected to increase sharply in the next few decades, leading to significant increases in health care costs. Finding new, effective treatments for both of these diseases is critical.

Alzheimer’s Disease

Alzheimer’s disease is characterized by the presence of amyloid beta plaque deposits between the nerve cells and neurofibrillary tangles of tau proteins inside the cells. While evidence linking the accumulation of amyloid beta plaque to Alzheimer’s disease resulted in the development of several therapies, none of them demonstrated clinical efficacy in clinical trials. Newer studies have been helpful in further understanding Alzheimer’s and have provided new targets for drug development. The public-private partnership for Alzheimer’s is focused on identifying new biomarkers for the disease that can predict clinical outcomes and conducting a large-sale analysis of human brain tissue from Alzheimer’s patients.

Members of the partnership are providing more than $185 million in funding and resources over five years for this research. Non-government partners include Biogen, GlaxoSmithKline, Eli Lilly, the Alzheimer’s Association, the Geoffrey Beene Foundation and USAgainstAlzheimer’s.

Parkinson’s Disease

Currently, available medicines manage the symptoms of Parkinson’s disease but none can reverse the effects of the disease or cure it. AMP members will focus on identifying promising biomarkers that might help doctors track the progression of Parkinson’s disease and lead to potential targets for new medicines.

Members of the partnership are providing $22 million in funding and resources over five years for this research. Non-government partners include Celgene, GlaxoSmithKline, Pfizer, Sanofi, the Michael J. Fox Foundation and Verily.

Sources:
2. Number of vaccines obtained through public, government and industry sources, and the Springer “Adis Insight” database. Current as of March 21, 2018. The medicines are either in clinical trials or undergoing regulatory review at the U.S. Food and Drug Administration.
4. American Brain Tumor Association
5. Alzheimer’s Association
6. National Health Survey, 2012, National Health Institute
7. National Institute of Neurological Disorders and Stroke, Chronic Pain Information Page
8. Parkinson’s Foundation
9. National Institutes of Health
10. Epilepsy Foundation
11. National Organization for Rare Disorders
12. Multiple Sclerosis Foundation
13. Migraine Research Foundation
14. American Heart Association
15. ALS Association