Testimony of Mark C. Trudeau
President and Chief Executive Officer
Mallinckrodt Pharmaceuticals
Before the House Committee on Oversight and Reform
October 1, 2020

Chairwoman Maloney, Ranking Member Comer, and Members of the Committee:

I am the President and Chief Executive Officer of Mallinckrodt Pharmaceuticals, a global specialty pharmaceutical company founded originally in 1867 with approximately 3,300 employees that develops, manufactures, markets and distributes a variety of specialty branded therapies as well as specialty generic products and active pharmaceutical ingredients for use in other medicines. Thank you for the opportunity to testify before you today.

I have been in the pharmaceutical industry for nearly 40 years. I began my career as a research and development engineer, and over the course of my career, I have worked on pioneering treatments for several critical diseases, including some of the very first for HIV. The leadership roles I have had in other regions of the world have allowed me to better understand both the strengths of the U.S. healthcare system and its challenges. I have devoted myself to this industry because I, like the thousands of other employees at Mallinckrodt, know that the therapies we make improve the lives of patients and their families.

This has been a year of unprecedented challenges. When COVID-19 hit, we mobilized to identify therapies to combat the disease. We consulted with the U.S. Food and Drug Administration (FDA) and National Institutes of Health (NIH) regarding potential evaluation of INOmax® – our inhaled nitric oxide therapy – for the treatment of COVID-19 related respiratory complications and supported an independent clinical trial being coordinated by Massachusetts General Hospital, the original and largest teaching hospital of Harvard Medical School. As of September 2020, nearly 250 hospitals and health systems in the United States have used INOmax as an experimental treatment for pulmonary complications in COVID-19 patients.

We also secured our supply chain to avoid manufacturing interruptions for the critical medications, active pharmaceutical ingredients and treatments we make, and donated 54,000 pieces of personal protective equipment, several ventilators and more than 16,000 gallons of hand sanitizer manufactured in our Missouri plant to locations across 47 U.S. states. We engaged with Members of Congress and federal agencies like the Biomedical Advanced Research and Development Authority (BARDA) to discuss leveraging our extensive experience producing

high-quality U.S.-made generics at our plants in Missouri, New York, Illinois and North Carolina to bring home the manufacturing of essential medicines and active pharmaceutical ingredients. Today, we are the only manufacturer of acetaminophen in the United States – a key active pharmaceutical ingredient in many medicines – which we proudly make in Illinois and North Carolina.

Our resolve to help patients has never been stronger, and we understand the American people's concerns over the availability and cost of medical treatments, particularly as the nation continues to combat the novel coronavirus pandemic and as patient out-of-pocket costs grow with increasingly higher deductibles in health insurance plans. We share those concerns and recognize that, if patients cannot obtain access to our therapies, we have failed in our mission. We are committed to ensuring that every patient with a valid prescription can obtain Mallinckrodt's innovative products, as will be discussed further below.

At Mallinckrodt, we believe that pricing for an innovative therapy should reflect the value that the treatment brings to patients, providers, and the healthcare system as a whole. As a leading producer of quality specialty generic pharmaceutical products with nearly a century and a half of expertise, we understand the importance of and necessity of supporting competition in the pharmaceutical market. We have never arbitrarily increased prices for any of our products and have pledged that, if we do increase the list price on any of our innovative therapies, the total change in a calendar year will not exceed single digit percentage points.

* * *

The Committee's inquiry has focused on, among other medicines, Acthar® Gel ("Acthar"), one of Mallinckrodt's most important – and yet least understood and often misunderstood – branded products. Acthar is a life-changing and life-saving therapy for many patients, some of whom are infants.

Acthar is a complex, injectable biopharmaceutical product FDA-approved to treat nineteen (19) serious conditions – devastating diseases like infantile spasms (a debilitating condition that if left uncontrolled can lead to long term neurological and cognitive damage), nephrotic syndrome, sarcoidosis, and uveitis, and refractory conditions like acute exacerbations of multiple sclerosis or rheumatoid arthritis. Not every patient needs Acthar, and treatment with it is episodic rather than chronic. With the exception of infantile spasms, for which it is the

Standard of Care, Acthar typically is a last resort treatment for a small subset population of patients and frequently prescribed when multiple other treatment options, including steroids, have failed. The majority of patients prescribed Acthar suffer from acute symptoms, and the average course of treatment can be relatively short: for example, for infantile spasms or the exacerbation of multiple sclerosis, the treatment period is often just weeks.

We are gratified that Acthar plays a critical role in improving the health and quality of life for these individuals, and we have been, and continue to be, committed to eliminating barriers to patient access. We support a free therapy and commercial co-pay assistance program for Acthar, both of which typically lead to patients paying nothing at all out of pocket. Under our stewardship, I am not aware of any infant in the United States who was prescribed Acthar for infantile spams and unable to be treated with it because of an inability to pay.

We have invested more than $660 million in Acthar since acquiring it in late 2014 to build clinical data confirming its safety and efficacy and to modernize its manufacturing process. Yet we have taken a responsible approach to pricing this important therapy and have made only modest adjustments to the list price. Under our ownership, the list price of Acthar has increased only around 5% annually, not factoring in inflation or the significant discounting that we have offered and that the prior owner did not. In two of the last six years, we made no change in price at all, and in 2019, the net price of Acthar went down, a trend we expect to continue in 2020.

One result of our significant investment in Acthar is a substantial body of health economics outcomes research demonstrating the value that Acthar has for the U.S. healthcare system. As is discussed below, treatment with Acthar has been shown to offset certain healthcare costs, including reductions in the utilization of both hospital and outpatient services across a number of indications. When prescribed as an intervening treatment before patients become even sicker, Acthar can reduce costly procedures or, as with infantile spasms, help patients avoid the challenges and financial strains associated with a lifetime of care.

Acthar often is a critical treatment of last resort, yet this medicine could easily have "disappeared" from the market were it not for the modernization of the compound that began in the late-1990s and has accelerated dramatically under our ownership. We believed at the time we acquired Acthar, and we believe now, that it has great potential to help more patients and that its potential has not been well understood. Acthar's potential could not be realized without the

significant clinical data analysis and manufacturing improvements in which we have been investing.

Additionally, as is true of virtually all pharmaceutical companies, revenue from Mallinckrodt's marketed products, including Acthar, makes possible research and development activities that can lead to breakthrough treatments that will produce real results for other patients in great need.

It is in large part because of Acthar that we have been able to build a robust pipeline of innovative products that, if approved, will give more patients suffering from difficult-to-treat and often overlooked conditions better treatment options. This includes Terlipressin, one of two treatments we are developing for patients suffering from advanced liver disease; StrataGraft®, our investigative regenerative skin therapy, which may reduce the need for autografting in certain burn patients, and for which, in August of this year, the FDA accepted our Biologics License Application (BLA) for review; Adrabetadex for Niemann-Pick Type C disease, a high mortality rare disease affecting children and adolescents; and, as previously mentioned, the potential use of INOmax as a treatment for pulmonary complications in COVID-19 patients. Acthar also helped fund our equity investment in Silence Therapeutics as part of a collaboration to develop and commercialize novel RNA[1] interference (RNAi) therapeutics for the treatment of serious diseases, including autoimmune diseases.

When engaging in any discussion about Acthar, I feel it is important to clarify several key facts about this unique therapy. First, there are ***already treatment alternatives*** for every indication for which Acthar is FDA-approved, and the media has reported that a number of companies are working on additional alternative medicines. Secondly, ***Acthar is not, and never to our knowledge has been, patent protected***. But it is a complex biopharmaceutical product that, similar to a biologic, is extremely complicated to manufacture. We have not, and are not, blocking potential competition to Acthar. It is our policy to provide reference samples of Acthar to potential generic manufacturers upon request. We have also supported legislation like the CREATES Act that ensures that potential generic manufacturers get appropriate access to samples.

* * *

Creating a Company Built for Innovation

In 2013, Mallinckrodt was a very different company – one resourced, skilled and focused on providing active pharmaceutical ingredients, generic medicines and diagnostic imaging compounds to the market through distributors.

As we became independent that year, our goal was something quite different – to transform into a science-based and innovation-driven biopharmaceutical company developing new therapies for seriously ill patients with hard-to-treat conditions who need new treatments. We set out to develop treatments for autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics and gastrointestinal products, while maintaining our foothold as a leading generic manufacturer and supplier of active pharmaceutical ingredients.

What may sound like a substantial but straightforward portfolio and pipeline evolution was far more complex. We embarked upon a multi-year, strategic business transformation that required us to simultaneously build the infrastructure necessary to operate a global public company, ***and*** create robust drug development, medical affairs and regulatory functions as well as sophisticated market access capabilities to ensure patient access to our innovative products. Simply put, we had to create a new company to support a new portfolio and do both essentially from scratch.

Over the next years, we reshaped our portfolio, divesting legacy divisions and products and acquired both marketed and development products that aligned with our new vision to address underserved patients and significant unmet clinical need. In this process, Mallinckrodt's organization, infrastructure, workforce and skill base underwent a metamorphosis.

As we built the branded portfolio, we steadily ramped up our investment in research and development. Today, we spend about $350 million on R&D annually. This is roughly 11% of our annual net income, and our focus on R&D continues to grow. We also established our presence in the hospital market (including by serving neonatal intensive care (NICU) patients) and in the market for rare treatment areas like immunology, nephrology, neurology, pulmonology and rheumatology.

We focused on building out a footprint for our R&D, regulatory, medical affairs and health economics research functions and state-of-the art branded development and manufacturing facilities – including one in Madison, Wisconsin, where StrataGraft, if approved early next year, will be manufactured. Manufacturing is of course one of our core areas of expertise given our nearly century and a half producing high-quality generic products and active pharmaceutical ingredients right here in the United States.

Without this transformation of our capabilities, and without the significant investments we have made in our infrastructure and manufacturing, Mallinckrodt would not today be providing innovative products like Ofirmev® (an acetaminophen injection used in hospitals), Therakos® photopheresis (innovative immunotherapy treatment platforms that enhance the ability of a patient's immune system to fight disease), Amitiza® (a leading global product in the branded constipation market), and INOmax to patients, nor would we be developing additional innovative therapies to serve more patients in need. But, most importantly to our discussion today, we could not have taken on the challenging task of modernizing Acthar.

As noted at the outset, Acthar has a long history. And today, despite myriad examples of Acthar having significantly improved the lives of patients, it remains one of the most poorly understood therapies on the market. I appreciate the opportunity to outline the important details of this medicine's evolution during this hearing.

The Acthar Story

The story of Acthar begins in the 1930s and 40s when a Mayo Clinic rheumatologist, Phillip S. Hench, M.D., was searching for a way to block or mitigate the ongoing joint damage inflicted by the human immune system in patients suffering from rheumatoid arthritis. In his work, he learned that another Mayo colleague, Edward C. Kendall, M.D., had isolated six hormones produced in the adrenal glands.

In the late-1940s, when one of the hormones (cortisone) was administered to a few patients, their symptoms subsided and demand for this potential treatment advancement skyrocketed. At the time, cortisone was hard to synthesize, so Dr. Hench began searching for another substance that would have the same clinical effect. He theorized that injecting another substance – adrenocorticotropic hormone (ACTH), which is made by the pituitary gland – might stimulate a patient's body to ***produce its own cortisone and other steroid hormones***.

Dr. Hench turned to another biological source of ACTH, porcine pituitary glands, and produced a compound for testing. When the substance was administered to the first arthritis patient in February 1949, the results were as good as those achieved with cortisone. In 1950, Dr. Hench, Dr. Kendall, and a third scientist were awarded the Nobel Prize in medicine for their discovery.

By 1952, a proprietary formulation process – which remains a trade secret today – was created and received FDA approval as "H.P. Acthar Gel." Thereafter, the therapy was launched and began to be used by physicians in a broad range of conditions. But by the 1980s, pharmaceutical companies had learned to synthesize steroids like prednisone, which became more commonly used than Acthar. Physicians ultimately focused the use of Acthar to treat exacerbations of multiple sclerosis or, in the case of pediatric neurologists, to treat infantile spasms.

Fast forward to 1995, when the FDA found numerous quality control problems at the Rhône-Poulenc Rorer (later Aventis) factory where Acthar was manufactured at the time. Rather than spend money on the substantial improvements needed to bring the manufacturing process up to the FDA's standards, Aventis announced that it would discontinue production of the therapy.

That decision created alarm among pediatric neurologists and some patient groups, and Aventis eventually agreed to continue making a limited supply of Acthar that would be reserved to treat infantile spasms or individuals suffering from relapses of multiple sclerosis. Unfortunately, given the extremely small number of patients suffering from these conditions and annual sales of only about half a million dollars, Aventis was losing several million dollars a year on Acthar.

In 2001, Aventis sold H.P Acthar Gel to Questcor Pharmaceuticals, which had to recreate and re-establish the complex manufacturing process used to make the therapy. To account for its manufacturing investments and to stabilize its finances, Questcor adjusted Acthar's price from around $40 a vial to $700 and instituted modest periodic increases after that.

In the time that had elapsed since the rise of synthetic steroids, and due to years of commercial neglect of Acthar, however, physicians had lost sight of its potential as a treatment option. Though Acthar's label remained broad, many physicians had no experience with it.

Prescribing remained extremely limited and the group of patients for whom Acthar was deemed an appropriate treatment incredibly small. While annual Acthar sales were about $12 million by the end of 2006, Questcor was hemorrhaging money.

In 2007, as reflected in contemporaneous SEC filings, Questcor was under increasing financial strain and concluded that its business model was not sustainable. To keep Acthar on the market and ensure its long-term supply to treat children afflicted with infantile spasms and other small groups of patients suffering from serious conditions, Questcor increased the price to $23,000 a vial. In 2010, following the completion of a modern clinical trial to evaluate the benefits of Acthar for treatment of infantile spasms, the FDA approved Acthar for treatment of this condition and awarded Questcor with seven years of orphan drug exclusivity. Additionally, the FDA reviewed the full body of data underlying the therapy and determined there was sufficient scientific and clinical evidence to support the effectiveness of Acthar in the other 18 different indications (aside from infantile spasms), each of which is now covered in the current label.

Modernizing Acthar

Mallinckrodt acquired Acthar in late 2014 because we understood it to be a treatment with greater potential that could play an important role in helping patients living with serious and often recurring conditions – for which steroids or other treatments do not work – lead healthier lives. We knew that there had been an under-investment in the therapy, and thus set out on a course to modernize it. Since taking ownership of Acthar, we have invested over $660 million to ensure that its full potential as a therapy for chronically ill patients can be realized.

These investments – which do not include sales and marketing expenses – have led to tangible outcomes. First, we have produced a much more detailed and precise characterization of the compound and its components, in addition to ACTH, and its unique mechanisms of action (which resulted in a 2019 label update by the FDA). Secondly, through a substantial program of clinical trials and health economic outcomes research, we have established a larger and growing body of evidence to support the efficacy and value of Acthar. Thirdly, we have undertaken manufacturing modernization, which is also generating new, more patient-friendly product presentations.

Our studies have given us deeper insights about the specific patient groups (in addition to children with infantile spasms) for which Acthar is most appropriate and beneficial – small groups of "refractory" patients with serious conditions for whom standard treatments have become ineffective or hard to tolerate. Our growing body of evidence includes case studies and independent investigator-initiated research, many funded by Mallinckrodt, conducted in major academic institutions by physicians who are experts in their fields, along with company-sponsored clinical trials and health economics outcomes research studies. During the brief time we have owned Acthar, we have initiated nine clinical trials targeting a combined enrollment of nearly 1,100 patients – a large number when one considers the generally small number of patients suffering from the conditions Acthar treats.

Last year marked the beginning of a significant and accelerating release of data from our clinical research and development programs. This included data from an investigator-initiated research study on the use of Acthar and its impact in uveitis patients, and positive top-line findings from an observational registry assessing relapse recovery in multiple sclerosis relapse patients treated with Acthar. It also included compelling data concerning the value of Acthar from a Phase 4 company-sponsored clinical trial of its use in patients with persistently active rheumatoid arthritis. The data showed that for such patients, treatment with Acthar resulted in low disease activity for an astounding 62% of patients ***for whom standard treatments did not work***. In 2019, we also enrolled the first patient in a Phase 4 trial of Acthar for severe keratitis – inflammation of the cornea that, if not timely treated, can lead to a loss of vision – and completed enrollment in a Phase 4 clinical trial of Acthar in lupus patients with difficult to manage disease.

In short, as we better understand Acthar, the better equipped we are to identify the patients for whom it is an appropriate treatment and to help physicians and payers appropriately and economically use the therapy.

Acthar's Value to Patients and the U.S. Healthcare System

At Mallinckrodt, we believe that assessing the value of a prescription therapy should be approached in a scientific manner that takes into account the impact the therapy has on the overall health of the patient; the impact (burden) of disease; the impact on society; and overall financial costs. Since 2015, we have invested in the completion of over 50 health economics and outcomes research (HEOR) initiatives that report real-world evidence and outcomes associated

with Acthar. The findings from these studies demonstrate that treatment with Acthar can lead to considerable cost offsets to the U.S. healthcare system, including a reduction in the utilization of both hospital and outpatient services across a number of indications.

For example, in one of our HEOR studies of patients suffering from multiple sclerosis relapse, the data shows that, with a lower total annual cost of care and a higher response rate, Acthar had a lower cost per response ($141,970) compared to alternative late-line treatments ($253,331). In another HEOR study relating to MS relapse, the findings confirmed that, while medication costs were increased in the treatment group that received Acthar, these costs were offset by 93% (among the cohort with 12 months of follow-up) and by 132% (among the cohort with 24 months of follow-up) by the relative decrease in inpatient and outpatient costs among the group treated with Acthar.

Our substantial investment in health economics outcomes research is but one more way we are working to modernize Acthar and ensure it brings value not only to the patients for whom it is the right – and sometimes only – treatment option, but also to the U.S. healthcare system. The more comprehensively we are able to map out which patients will benefit most from Acthar, the more savings we can generate for the healthcare system overall. This is one of our enduring goals.

* * *

Mallinckrodt Today and In the Future

As I mentioned at the outset, the past year has been an eventful one for Mallinckrodt. We advanced a number of innovative therapies in our development portfolio. We presented positive top-line results for Terlipressin, a therapy that is being studied in patients with hepatic renal syndrome 1 (HRS-1), a life-threatening, rare disease that leads to kidney failure. With no approved treatment in the United States for this difficult-to-treat syndrome, we recognize how vital a therapy Terlipressin may be for patients experiencing it. In July of this year, an FDA advisory committee gave Terlipressin a positive recommendation for approval. Nonetheless, earlier this month, we received a Complete Response Letter (CRL) from the FDA stating that the agency needs more information to support a positive risk-benefit profile. While we are disappointed with the FDA's response, we are confident in the strength of the data from Terlipressin's Phase 3 CONFIRM study – the largest clinical trial ever conducted in this rare

condition. As every innovative pharmaceutical company knows, the road to drug approval is often a challenging one. We are committed to working with the FDA to evaluate next steps in an effort to ultimately receive approval of this important therapy.

And, as mentioned earlier, we are looking forward to a successful conclusion of the FDA's review of the StrataGraft BLA. In addition, we are continuing to work with the FDA on a potential path forward for Adrabetadex to treat Niemann-Pick Type C disease; we are evaluating the use of INOmax as a supportive measure for treating coronavirus-associated lung complications; and we are working towards the completion of a new self-injection device for Acthar, which will be an important advancement for patients and the product. We are excited about the potential for these new, innovative treatments and presentations to complement our existing brands portfolio that includes Ofirmev, Therakos and Amitiza.

During the past year, we also made progress developing additional applications for our existing brands products. This includes reporting top-line results from our proof of concept study of nitric oxide gas in ex-vivo system of human lungs showing an increase in oxygenation and the duration "out-of-body" perfusion; announcing the approval of INOmax in Australia for treatment of pulmonary hypertension in adults in conjunction with cardiovascular surgery; and announcing the results of an independent-investigator study demonstrating the effectiveness of Therakos ECP therapy as an adjunct to standard therapy in treatment of lung cancer patients with Bronchiolitis Obliterans Syndrome.

And we continue to have a leading specialty generics business that builds upon our century and a half of manufacturing expertise in the United States centered on quality, integrity and service. We have been manufacturing active pharmaceutical ingredients for over 120 years across multiple U.S. sites. We currently operate America's largest active pharmaceutical ingredient site by volume in St. Louis with 49 Drug Master Files (DMFs). While large, our generics manufacturing operation remains nimble. When the coronavirus pandemic took root in our country earlier this year, we quickly converted one of our U.S. manufacturing lines to produce isopropyl alcohol-based hand sanitizer that we continue to make available for donation across the country today, with direct shipments of 16,000 gallons and counting to locations across 47 states so far. This effort is just one example of our specialty generics business rising to the call of a national emergency. After the Three Mile Island nuclear disaster, the federal

government ordered one-quarter of a million doses of potassium iodide from Mallinckrodt to aide in the response. The first shipment arrived within 24 hours, and the full order was fulfilled within five days.

Our specialty generics operation also remains focused on developing new generic medicines, with multiple products in the pipeline that will improve patient access to more affordable medications. Combined with our active pharmaceutical ingredient capabilities and both small- and large-scale finished-dosage capabilities, our specialty generics operation is second-to-none in terms of agility, ability and quality.

* * *

While Mallinckrodt's transformation into a science-based company developing new therapies for seriously ill patients with hard-to-treat conditions is not yet complete, and we have challenges to navigate, we are well on our way. We have built the infrastructure and cultivated the talent needed to develop and bring to market innovative treatments for complex diseases and serious conditions. We remain unwavering in our determination to find new solutions for sometimes old, and often overlooked conditions that keep patients from living their best lives, while continually working to improve patient access to our innovative products and producing more affordable specialty generic medicines.

Thank you again for the opportunity to appear before you today.