Catalyst pharmaceuticals

Patrick J. McEnany
Chairman and
Chief Executive Officer

February 21, 2019

VIA E-MAIL AND FEDERAL EXPRESS
Senator Bernard Sanders
332 Senate Dirksen Office Building
Washington, DC 20510

Re: Response to your letter dated February 4, 2019

Dear Senator Sanders:

We have received your letter dated February 4, 2019, in which you seek information about our development and commercialization of Firdapse®, the first and only FDA-approved, evidence-based therapy for the treatment of adults with Lambert-Eaton Myasthenic Syndrome ("LEMS"), an ultra-rare autoimmune disorder, most often characterized by fatigable limb muscle weakness. We thank you for your interest in the LEMS community. However, we believe it is important that we help you fully understand our extensive work in evaluating Firdapse® (amifampridine phosphate) that led to an FDA approval of our product. As was evidenced in your public interview with a LEMS patient, access to Firdapse® can be life-changing for someone with this devastating disease, allowing a patient to resume his or her role as a productive member of society. The approval of Firdapse® by the FDA means that ***ALL*** LEMS patients in the United States now have access to this much-needed medication.

Executive Summary

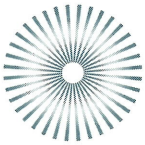
The following summarizes several points that we believe are important for you to understand:

- There was a large unmet medical need for an FDA approved therapy to treat LEMS patients. Prior to initiating our development program for amifampridine phosphate, only about 200 LEMS patients were receiving an unapproved, investigational amifampridine product to treat their disease. Since the estimated prevalence of LEMS in the U.S. is about 3,000 patients, the vast majority of LEMS patients did not have access to an amifampridine-based product. With FDA approval, all adult LEMS patients (and not just a few) now have affordable access to Firdapse®.

- Catalyst has developed an array of financial assistance programs that are available to reduce patient co-pays and deductibles to a nominal affordable amount and, since the approval of Firdapse®, a physician can now simply write a prescription and Firdapse® will be delivered to the patient's door within 2-3 days and in most cases the patient's monthly out-of-pocket expense will be $10 or less.

- While a few patients may have had access to unapproved, investigational amifampridine, Firdapse® is not an "old drug" or a repurposed drug. Until Firdapse® was approved, an amifampridine-based product had never been approved in the U.S. for any indication, and thus our product has received a new chemical entity designation from the FDA.

- In order to gain FDA approval of our product, we were required to submit the results of more than 70 non-clinical and clinical studies, including two Phase 3 trials evaluating Firdapse® for the treatment of LEMS, at a cost of millions of dollars. Based on the evidence we presented, in November 2018 the FDA approved Firdapse® (amifampridine phosphate) for use in adults with



LEMS. Now, for the first time, LEMS patients have confidence that their therapy is FDA approved and is safe and effective.

- Catalyst continues to spend millions of dollars per year evaluating Firdapse® in clinical trials as a potential treatment for other rare neuromuscular disorders where there is no current FDA approved drug to treat those disorders. Those conditions include congenital myasthenic syndromes (1,000-1,500 patients), MuSK antibody positive myasthenia gravis (3,000-4,800 patients), and spinal muscular atrophy Type 3 (2,000-2,500 patients). While we are hopeful, we have no guarantees that our investment in the clinical trials for these other indications will be successful.

- We respectfully question the notion that the use of an experimental product not approved by the FDA is an acceptable standard of care for LEMS patients – or indeed for any patients. This means of "distribution" was **never** intended to be a final or even a long term mechanism for making drugs available to patients under the law. Such a notion represents a dangerous precedent that runs counter to the entire FDA regulatory structure.

Background on Catalyst Pharmaceuticals and Firdapse®

Catalyst, founded in 2002, is a biopharmaceutical company dedicated to researching, developing and providing access to FDA approved innovative treatments for ultra-rare debilitating, chronic neuromuscular and neurological diseases. Our senior management team has decades of clinical research experience, with a particular focus on neurological and neuromuscular disorders. We currently have more than 50 employees, and through the contractors who help us meet the needs of patients, we bring jobs to hundreds of people in the United States.

The chemical name of Firdapse® is amifampridine phosphate. Its active ingredient is 3,4-diaminopyradine (sometimes called 3,4-DAP)[1]. In October 2012, to expand our research on drugs to help patients with unmet medical needs, we licensed the North American rights to Firdapse® from BioMarin Pharmaceuticals ("BioMarin"). Our work and personnel have been focused on bringing to the entire LEMS community the first FDA-approved, evidence-based therapy for this rare and debilitating disease. We note that Catalyst did not use NIH or other public funding to develop the drug, and our path to the development and approval of Firdapse® is entirely consistent with the extensive clinical and non-clinical programs required to develop any pharmaceutical product.

With respect to Catalyst's efforts to obtain approval of Firdapse® for LEMS, it is important to recognize that any other pharmaceutical company that was willing to take on the financial risks associated with making an investment in this product could have done so because amifampridine is a molecule without patent protection.

Prior to our obtaining the North American rights to Firdapse®, our drug had been granted orphan drug exclusivity by the FDA. We also obtained "breakthrough therapy designation" from the FDA for our drug in 2013. Both designations signal FDA's affirmation that the product was important and worthy of evaluation for treatment for this serious, ultra-rare condition, and that if Catalyst focused its efforts and expertise on the opportunity, along with bearing the associated financial risk, to evaluate amifampridine phosphate to the point where it could be approved by the FDA, it would be entitled to the benefits afforded

[1] While our product shares the same chemical entity with what is known as "free base amifampridine," Firdapse® is formulated to include the phosphate salt of amifampridine, distinguishing it from other formulations. Unlike the freebase product, our product provides LEMS patients with the assurance that the amifampridine salt consistently delivers the correct potency and purity without the need for constant refrigeration. Prior to our product's FDA approval, this instability (with reported variable potency) and constant need for refrigeration presented concerns and limitations for LEMS patients utilizing the unapproved, non-salt amifampridine formulation.

by the Orphan Drug Act of 1983. Orphan Drug exclusivity means that the FDA has determined that the drug is intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States. The Orphan Drug designation, and the marketing exclusivity that it provides, was Congress' way of incentivizing pharmaceutical companies to take the risks associated with developing and obtaining approval of drugs used to treat ultra-rare conditions.

Providing LEMS patients with an approved, efficacious and safe product

FDA approval of pharmaceutical products is the 'gold standard' upon which U.S. society and other developed countries rely, signaling a drug has met the FDA's stringent approval requirements, including a demonstration of safety and efficacy, and is widely available for use by physicians treating patients. There is universal agreement that FDA approval of amifampridine ensures that physicians and patients have access to a drug manufactured according to FDA current good manufacturing practice regulations with stable, consistent potency. FDA approval also provides the benefits of FDA approved labeling, including clear prescribing and drug safety information, as well as pharmacovigilance (ongoing monitoring of drug safety and quality). FDA approval allows for legally educating and broadly publicizing the clinical benefits and availability of such a medicine to patients and physicians. We strongly believe that awareness of the disease in both the physician and patient communities will improve significantly now that there is an FDA approved version of amifampridine, as FDA approval assists in elevating the public recognition of this rare disease and helps to ensure that patients with LEMS are properly and quickly diagnosed and treated.

In order to gain FDA approval of our product, we were required to submit the results of more than 70 non-clinical and clinical studies, including two Phase 3 trials evaluating Firdapse® for the treatment of LEMS[2], at a cost of millions of dollars. We also had to demonstrate compliance with FDA's manufacturing regulations and assure FDA that we could manufacture Firdapse® with acceptable stability and consistent potency, which cost additional millions of dollars. Based on the evidence we presented, in November 2018 the FDA approved Firdapse (amifampridine phosphate) for use in adults with LEMS. Now, for the first time, LEMS patients have confidence that their therapy is FDA approved and is safe and effective. This is what Catalyst believes U.S. drug companies have a moral and ethical obligation to do: to evaluate the safety and efficacy of potential pharmaceutical products and meet the high standards required to obtain approval of previously unapproved drug candidates from the FDA.

As has been publicized, Jacobus Pharmaceuticals[3] has been providing the free base form of amifampridine to a limited number of LEMS patients for nearly 30 years as an investigational, experimental drug under the FDA's investigational new drug (IND) process. It should be noted that Catalyst also has been providing Firdapse® for about five years at no cost to patients as part of our expanded access program, which was created under our IND as we worked on the clinical and non-clinical development of the drug. The purpose of a compassionate use program or an expanded access program (both of which are the same) is to allow dispensing of experimental, investigational, unapproved drugs to patients for a limited period of time; specifically while companies undertake the necessary steps to obtain FDA review and approval. Further, FDA's IND regulations expressly prohibit providers of these experimental drugs from charging patients for them, unless granted approval to charge by the FDA; thus, such drugs are typically provided at no cost to the patient.

---

[2] While you appear to be suggesting in your letter that Catalyst has done minimal product development on Firdapse®, you should recognize that, in fact, Catalyst has done more to obtain the approval of Firdapse® than is typical of many orphan drugs because Catalyst conducted two well-controlled Phase 3 clinical trials in order to obtain FDA approval of Firdapse®. In many cases, orphan drugs are approved by the FDA based on only one such Phase 3 clinical trial.

[3] For reference, Jacobus filed an IND for amifampridine in the early 1990s and received orphan drug designation for amifampridine in 1999.

Compared to the process of obtaining an FDA-approved product, the process of obtaining an investigational, experimental drug under a compassionate use IND differs significantly from what most U.S. patients experience when diagnosed with a medical condition – going to a physician, obtaining an appropriate prescription, and filling it at a pharmacy. Physicians who desire to prescribe experimental drugs under INDs undergo a cumbersome process to do so, and the fortunate few patients who become aware of the program may be required to travel hundreds of miles to have access to the limited number of physicians willing to participate in a compassionate use program for a rare disease. This effort is notable and separate from the fact that many physicians and LEMS patients were either not aware of, or unable to access, amifampridine due to the costs and obstacles to IND participation. While the FDA has taken steps over the last few years to reduce the burden and improve patient access under compassionate use programs, compliance with these programs remains cumbersome for both physicians and patients (understandably, due to these drugs being experimental and not approved by the FDA).

However, we note again that the use of an experimental product not approved by the FDA should not be the acceptable standard of care for LEMS patients – or indeed for any patients – in any situation. This means of "distribution" was intended only to cover the period while companies undertook the necessary steps to obtain FDA review and approval of the drug product, and was never intended to be a final or even a long-term mechanism for making a drug available to patients under the law. Such a notion represents a dangerous precedent that runs counter to the entire FDA regulatory structure.

Further, your letter appears to suggest that the LEMS community has been adequately served by the availability of this drug as an unapproved, experimental product. There are approximately 3,000 adult patients in the United States with LEMS, of which, based on our review of epidemiology studies, health care claims transactions and hospital discharge data, approximately 1,500 patients have been diagnosed with LEMS in claims data over the last two years. This estimate of the diagnosed patient population compares favorably with the epidemiology studies in the literature and reflects the fact that, as is often the case with ultra-orphan diseases, many of these patients are misdiagnosed or undiagnosed[4].

We estimate that (prior to our development program) within the compassionate use program previously operated by Jacobus, only about 200 of the estimated 3,000 LEMS patients in the U.S. were on investigational amifampridine. That meant that the vast majority of LEMS patients were without treatment for this debilitating disease until our drug was approved for commercialization. It is inappropriate to imply that the entire LEMS patient community was being effectively treated with an investigational drug.

As part of its approval of Firdapse®, the FDA is requiring Catalyst to spend millions of additional dollars to conduct additional post-approval studies of our drug product to further characterize the drug's safety. Additionally, our development mission to help patients does not end with the approval of Firdapse® for LEMS. We are also continuing to rigorously evaluate Firdapse® in clinical trials for the treatment of other rare neuromuscular diseases such as congenital myasthenic syndromes, MuSK antibody positive myasthenia gravis, and spinal muscular atrophy type 3, and we are excited about the possibility that this drug can help others with rare diseases in a similar way that we see clinical benefits for those suffering from LEMS.

[4] Some of the factors that affect the size of the population with a rare disease such as LEMS include the number of patients actually diagnosed with the disease, the number of patients who are misdiagnosed with other diseases, and the number of patients who are simply undiagnosed. Additionally, while there is an antibody test that positively identifies patients with LEMS, the test is not particularly well known or utilized at this time by many neurologists. Further, many LEMS patients who have small cell lung cancer (SCLC) are not being treated for LEMS because many oncology medical professionals who treat SCLC patients are generally unfamiliar with how to diagnose and treat LEMS. All of these factors affect the ultimate number of patients who will benefit from treatment with Firdapse®.

Supporting LEMS patients being treated with Firdapse®

At Catalyst, our focus is on our patients, and improving their care is our number one priority. We recognize that the journey from symptom onset to LEMS diagnosis can be long and frustrating, often taking many years. We are expanding our efforts to work tirelessly with the LEMS community to raise awareness, encourage accurate and timely diagnosis, and accelerate early intervention and access to treatment that can provide patients relief from the debilitating symptoms of this serious and life-threatening disease.

In January 2019, we launched Firdapse® in the U.S., marketing the product through a field force with extensive experience with neuromuscular, central nervous system, or rare diseases products. Our team includes specialists in patient assistance, insurance navigation support, and payer reimbursement support. We also have a field-based force of medical science liaisons who are helping educate the medical community and patients about LEMS and about our company's ongoing clinical trial activities. Further, we work closely with several rare disease advocacy organizations (including Global Genes, the National Organization for Rare Disorders (NORD), and the Myasthenia Gravis Foundation of America) to help increase awareness and the level of support for patients living with LEMS, CMS and MuSK antibody positive myasthenia gravis, and to provide education for the physicians who treat these rare diseases and the patients they treat.

In order to help patients afford their medication, we, like other pharmaceutical companies who are marketing drugs for ultra-orphan conditions, have developed an array of financial assistance programs that are available to reduce patient co-pays and deductibles to a nominal affordable amount. For eligible patients with commercial coverage, a co-pay assistance program designed to keep out-of-pocket costs to $10 or less per month is available for all LEMS patients prescribed Firdapse®. We are also donating, and committing to continue to donate, money to qualified, independent charitable foundations dedicated to providing assistance to LEMS patients in financial need. Our goal is to ensure that no LEMS patient is ever denied access to Firdapse® for financial reasons.

We are supporting the distribution of Firdapse® through "Catalyst Pathways," our personalized treatment support program. "Catalyst Pathways" is a single source for personalized treatment support, education and guidance through the challenging dosing and titration regimen to an effective therapeutic dose. It also includes distributing the drug through a very small group of exclusive specialty pharmacies (primarily AnovoRx), which is consistent with the way that most pharmaceutical products for ultra-orphan diseases are distributed and dispensed to patients. By using specialty pharmacies in this way, the difficult task of navigating the health care system is far better for the patient needing treatment for their rare disease and the health care community in general.

In addition, "Catalyst Pathways" is the gateway for our free bridge medication for patients during transitioning from investigational product while they are waiting for a coverage determination or, later on, for patients whose access is threatened by the bureaucratic complications arising from a change of insurer. The "Catalyst Pathways" program is also the access point for our Patient Assistance Program, which provides longer-term free medication for those who are uninsured or functionally uninsured with respect to Firdapse® because they may be unable to obtain coverage from their payer despite having health insurance.

We have established pricing for Firdapse® at an annual list price of $375,000 for a typical LEMS patient who remains 100% persistent and compliant with therapy for an entire year. We believe that the pricing of our product is in line with the pricing of other products that provide significant clinical benefits in treating an ultra-orphan disease of similar severity and in order to properly compensate companies for the costs associated with developing, manufacturing, and marketing an orphan drug in compliance with regulatory requirements. We believe that our drug will be widely covered and reimbursed by private and public payers for the indicated small population of adult LEMS patients, as part of their mission to assure that rare disease

patients receive timely treatment for proven medicines. Furthermore, forecasted rebates, discounts, patient commercial co-pay support, Medicare coverage gap subsidies, statutory Medicaid discounts and other governmental discounts will result in our net sale price being 15-20% lower than our annual list price for the product.

We are focused on helping all patients in the LEMS community

As noted above, we have had the privilege of working with the LEMS community for several years, and we believe that our efforts on behalf of that community have helped advance the visibility of this patient group that has been largely unrecognized and unmet in the wider medical community and society. We regularly speak with LEMS patients who reach out to us to share their patient journeys. We are carefully listening to all of these patient stories, and we use those interactions to continuously improve our services to LEMS patients and the neurologist and neuromuscular physician communities. If patients or their physicians with whom you speak are concerned, I welcome them to contact me personally and I will do everything I can to help make their journey as stress free as possible – that is what we are committed to doing and have been doing at every turn. Furthermore, we would be happy to introduce you to LEMS patients who will share their personal stories and how well they have been treated by Catalyst, as well as how effective Firdapse® has been in treating their LEMS symptoms.

Again, Senator Sanders, thank you for the opportunity to dialogue with you on our common commitment to improving healthcare for all Americans.

Sincerely,

Patrick J. McEnany
Chairman and CEO