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**U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH**

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“EXAMINING PATIENT ACCESS TO EXPERIMENTAL DRUGS”

Chairman Burgess and Ranking Member Green, Members of the Committee, my name is Kenneth Moch, President and Chief Executive Officer of Cognition Therapeutics, headquartered in Pittsburgh, Pennsylvania. Thank you for having me here today. This hearing is looking at patients' access to experimental drugs, and I have a great deal of experience with expanded access from my roles in leadership at small, innovative biotechnology companies.

I have spent my career at the interface of science and business, having been the CEO or co-founder of 5 biotechnology companies focused on developing new medicines for life-threatening diseases, including Alzheimer's disease (Cognition), the first liposome company, the first cord blood stem cell bank and, prior to Cognition, an antiviral therapeutics company called Chimerix. In my years building and leading emerging biotechnology companies, I have overseen several expanded access programs, and in my position as a Board Member for the Biotechnology Innovation Organization (BIO), I have

engaged with many other CEO's to draft principles for expanded access programs.

While I am a strong supporter of expanded access programs, I am NOT a supporter of Right to Try legislation. In my opinion, this is feel-good legislation which gives false hope to patients in need, without actually helping them.

There are few issues with more emotional and moral impact than "Right to Try." I applaud the Committee for its willingness to examine this issue in depth, from all perspectives. While the idea of a patient's "right to try" has become a very popular idea in this country and, since 2014 37 states have passed "right to try" laws and the U.S. Senate passed legislation earlier this year, there is shockingly little discussion about the social, ethical and moral conflicts and dilemmas in the use of experimental medicines to treat life threatening medical conditions.

For patients and their loved ones, there is no moral quandary. They want access to a drug they believe could save or extend their life. I fully understand that. All of us, if we had a family member who was critically ill – a child, a parent, a sibling - or if we were critically ill ourselves, would do everything in our power to gain access to any experimental medicine that

might increase the chance of survival. That being said, for the company engaged in the drug development, the Food and Drug Administration (FDA) and lawmakers, it is our moral imperative to not just think of that one patient, but of all the patients. We must consider, beyond the risks to an individual, how does society or a company balance the immediate needs of a critically ill individual, in many cases a child, versus the potential needs of many future patients?

In 1987, mostly in response to the AIDS crisis, the FDA instituted expanded access guidelines where an unapproved medicine could be made available to an individual with a serious or immediately life-threatening disease. In 2009, the guidelines were substantially revised and three categories of use were outlined. With the revision, the FDA was seeking to balance the desire of sick and vulnerable patients to get access to drugs with safety and without compromising the clinical trials process. The FDA's statement on this topic: *"Expanded access, sometimes called "compassionate use," is the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options. The drug manufacturer and the patient's doctor must make special arrangements to obtain the drug for*

*the patient. These arrangements must be authorized by the FDA. These safeguards are in place to avoid exposing patients to unnecessary risks.”*¹

In practice, however, the FDA's role is not always as clear. According to Richard Klein, former Director of FDA's Patient Liaison Program, the FDA's role is to provide a “mechanism” for expanded access. Indeed, the FDA approves over 99% of the requests it receives for expanded access. From 2009 to 2013, the period of time when Chimerix first had an expanded access program, the FDA approved 4017 expanded access requests, both individual patients and larger expanded access protocols, and denied 24. In 2014 the FDA approved approximately 2000 more requests. While the number of IND submissions and protocol requests declined in 2015 and 2016, the approval rate remains at a similar percentage.

Given that the FDA only processes an expanded access request when it has been received from the drug's sponsor, almost always a company which is developing the experimental medicine, what these approval percentages clearly illustrate is that the decision as to whether or not to grant an expanded access request falls to the leadership of the company developing the new medicine, not the FDA.

¹ Access to Investigational Drugs Outside of a Clinical Trial (Expanded Access). <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccessToInvestigationalDrugs/ucm176098.htm>; Statement language is from May 2014, at the time of the #SaveJosh social media campaign.

For companies, decisions around whether to grant or deny expanded access requests are heart wrenching. In many circumstances, it is making the decision around practical aspects of drug approval and the desire to treat all the patients with an approved medicine, against an emotional plea from a patient who is out of options. Additionally, there are regulatory and legal implications for companies in their decision to grant or not grant preapproval access to experimental medicines.

First and foremost, a biotechnology company's top priority is getting a drug through the FDA approval process, so that it is available to ALL patients. We cannot lose sight of that mission in this discussion, and "right to try" cannot supplant this mission. We must continue to work to innovate clinical trials and streamline the FDA approval process so that drugs can make it to market quickly and safely. I applaud this Committee for their efforts in this regard. Both 21St Century Cures and The FDA Reauthorization Act will move this forward.

Second, a company may not be willing or able to take the risk of providing its experimental drugs to patients due to legitimate financial and personnel constraints that prevent them from doing so—particularly for small companies. While this may sound cruel against the plea from a dying

patient, the experimental medicine may simply not be well enough understood to be provided outside of the confines of well controlled clinical testing.

It is important to always remember that in developing new medicines you are attempting to alter a biochemical process in a finely tuned organism called human beings that took millions of years to evolve, and you're trying to do so without having effects that are outside of your specific target process.

No ethical company that I know of would ever release an experimental medicine outside of the FDA's regulatory process. A basic mantra is that "all drugs have side effects." Right to Try legislation has been written with the assumption that the safety of an experimental medicine is well characterized after initial Phase 1 testing, and the clear evidence is that this is simply not the case. Nor is the efficacy of an experimental medicine well understood after Phase 1 testing. Yes the issue is the risk/benefit profile of a critically ill or terminally ill patient, but this decision must be made on a case by case basis for each experimental medicine as it is developed.

Additionally, there are circumstances where companies do not have the resources, the experimental medicine itself or the personnel to provide oversight, to simultaneously conduct clinical trials and participate in expanded access.

I often say that biotech companies are “research and development pipelines unencumbered by revenue” – we conduct years and often decades of research and development on unproven experimental medicines, and spend hundreds of millions and often over a billion dollars in investment capital before hopefully reaching FDA approval and generating product revenue. The practical result of this is a fragility of the company and limited resources that must be dedicated to getting the product to approval. Additionally, expanded access programs require dedicated, trained personnel to handle requests, assist requesting physicians, dispense the drug, field questions, and handle paperwork and reporting, and many companies simply cannot handle this additional personnel and workload.

Third, the company has to consider the ramifications of a critically ill patient that gets worse or dies, related or unrelated, to the experimental drug. This can cause other patients to decline to participate in clinical trials, or put the approval of the product in jeopardy. Giving experimental medicines to critically ill individuals under less or in some cases completely uncontrolled

conditions is inherently risk creating. With the increasing awareness of expanded access, heightened by the Right-to-Try legislation, individuals are likely to be asking for experimental medicines earlier in the development process and for conditions that are further separated from the primary conditions for which the medicine is being developed. If things go badly, future patients might not receive a needed medicine because FDA approval is derailed or delayed. Biotechnology companies, the FDA and legislators must advocate for the needs of those patients as well.

Finally, the role of social media must be considered, as it is interlinked with the explosion of "right to try" laws. In the era of Facebook and Twitter, where people can express their opinions and interact with others in real-time, the moral and ethical issues created by these situations are complicated by a hyper-immediacy that increases the intensity and scrutiny under which these issues must be addressed.

I have had very personal experiences with this. My former company, Chimerix, Inc., went through a very public ordeal with a young boy whose parents undertook a social media campaign which resulted in extreme pressure on Chimerix to grant access to an experimental antiviral drug.

Chimerix was founded in 2002 to develop an oral form of a potent intravenously administered antiviral drug as a medical countermeasure against smallpox. At the time that I joined Chimerix in June 2009, the company was beginning to expand its development program to look at the potential for its drug, brincidofovir, to treat other viruses within the double-stranded DNA viral family, including herpes viruses such as cytomegalovirus, papilloma viruses, polyoma viruses and adenovirus. Soon thereafter, the decision was made to focus the Company's clinical development efforts on the potential use of brincidofovir to prevent the reactivation of cytomegalovirus in bone marrow stem cell transplant recipients, a pathological event that was known to significantly increase post-transplant mortality.

The first compassionate use of brincidofovir occurred in March 2009, when Chimerix provided brincidofovir to help save a soldier who, after receiving a smallpox vaccination, had a life-threatening breakthrough of the vaccinia pox virus. From this single event and the subsequent publication by the Center for Disease Control in May 2009², interest in and requests for brincidofovir grew through word of mouth within the medical community and led to a significant expanded access program by Chimerix.

² Progressive Vaccinia in a Military Smallpox Vaccinee --- United States, 2009. CDC Morbidity and Mortality Weekly Report, May 19, 2009. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm58e0519a1.htm>

Starting in September 2009, approximately 50 individual requests for brincidofovir were received over a 9-month period, increasing to approximately 50 requests over next 3-month period. This was one of the largest individual patient expanded access programs undertaken by a biotech company, at its peak accounting for an estimated 6% of the expanded access request to the entire FDA and an estimated 30% of the requests to the Antiviral Drugs Division. Because of this, in late 2010 the FDA asked Chimerix to establish a formal "intermediate size" Expanded Access program that would be listed on clinicaltrials.gov.

In February 2011, Chimerix received an \$88.1 million contract from the Biomedical Research Advanced Development Authority (BARDA), a portion of which was designated to pay for the 200-patient clinicaltrials.gov expanded access protocol in order to gain insights into emergency situations which were closely analogous to a potential smallpox outbreak. In late 2012, when funding under the BARDA program ended, Chimerix closed the expanded access program for brincidofovir to focus its resources on the formal regulatory approval process. At the time, Chimerix was still a private company, and had limited financial resources.

In total, brincidofovir was provided via expanded access to approximately 430 patients [215 individual requests plus 215 under the BARDA funded

program] to treat many different dsDNA viruses. During 2013 into 2014, after the cessation of the brincidofovir expanded access program, more than 300 additional requests were received and denied by the Chimerix Medical Department.

On February 12, 2014, doctors at St. Jude Children's Hospital in Memphis requested that Chimerix provide brincidofovir for a seven-year-old patient, Josh Hardy. Josh Hardy had been diagnosed at the age of 9 months with a malignant, highly aggressive, and rare form of kidney cancer. He subsequently survived three other bouts of cancer but, as a result of the treatments he had earlier in his life, in November 2013 a bone marrow biopsy revealed that he had a bone marrow failure. On January 10th, 2014, he received a bone marrow transplant at St. Jude Children's Hospital in Memphis, Tennessee. While he had heart and kidney issues before, the transplant caused further complications. Several days after the bone marrow transplant later, he was moved to the ICU for heart failure and five days later was put on a ventilator. He then developed an adenovirus infection as a result of his compromised immune system. As a result, Josh's doctors recommended that he receive brincidofovir under expanded access.

At that time, Chimerix had 55 employees. The expanded access program had closed and all of the resources were focused on completing the ongoing

Phase 3 clinical trial. Therefore this request, as with the hundreds before it, was denied by the Chimerix Medical Department.

Another request was made on March 5th by the St. Jude's Vice President, Clinical Trials Administration stating that "it is likely that after having fought against childhood cancer for so long, he may succumb to this infection without a non-nephrotoxic medication with superior efficacy proven in clinical trials." This second request was also denied.^{3,4}

It is at this moment that the importance of adhering to the process of developing new medicines intersects with the expanding world of a patient's "right to try" to get access to preapproved drugs. And while none of the policies being discussed in the states or at the Federal level would force companies into giving patients experimental drugs, they do work to encourage situations that we quickly found ourselves in at Chimerix.

On March 6th, one day after the second denial, Josh's mother Aimee Hardy wrote the following post on her Facebook page:

³ Facebook, #SaveJosh, March 7, 2014.

<https://www.facebook.com/SaveJoshHardy/photos/pcb.666481523393017/666481483393021/?type=1&theater>

⁴ Young cancer survivor's family pleads with company for experimental drug, Ryan Jaslow, CBS News, March 11, 2014
<http://www.cbsnews.com/news/young-cancer-survivors-family-pleads-with-drug-company-chimerix-for-experimental-drug/>

"Our son, Josh Hardy, who recently had a bone marrow transplant has developed the adenovirus. This [is] a deadly virus for people who have weak immune system[s]. There is a drug called Brincidofovir that has been proven to treat the adenovirus effectively. Our doctor at St Jude told us they ran the study for the drug company and he knows it will work. However, the drug company has refused to release the drug for compassionate care because they are trying to take it to market. Basically they are not going to save a child's life for money. The company is Chimerix Inc out of Durham, NC. And the main contact is Dr. Herve Mommeja-Marin. And the drug is called Brincidofovir. The child that absolutely needs it to save his life is Josh Hardy. He is currently in the ICU at St Jude Children's Research Hospital. If anyone with influence can help us convince the Chimerix Inc to release the drug for compassionate care for our son, we would be forever grateful. The phone # of Chimerix Inc is 919-806-1074 and the email is compassionateuserequest@chimerix.com"⁵

Mrs. Hardy posted her plea for help on another website, Caringbridge:

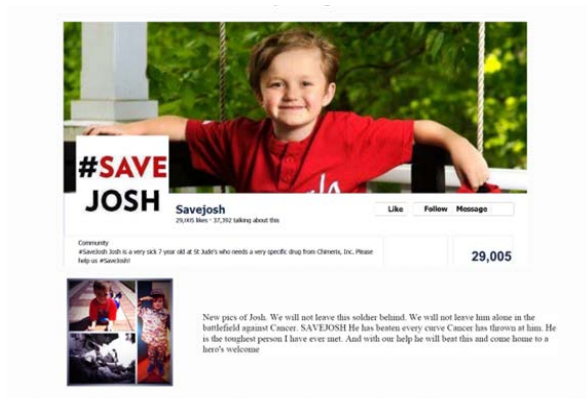
"We are asking everyone to think of any US representatives they might know or pharmaceutical connections that might help us. If

⁵ Aimee Hardy Facebook page. https://www.facebook.com/aimee.hardy.5?hc_location=timeline

anything, if 500 people or so just called Chimerix and told them they should send the Brincidofovir to Josh Hardy at St Jude's, it might be helpful"⁶

Overnight, into the morning of March 7th, Josh Hardy's uncle created a Facebook page and twitter campaign called "#SaveJosh." (Figure 1) His first post on the Facebook page was the letter from St. Jude's Vice President to Chimerix containing the second request for brincidofovir.

Figure 1, the #SaveJosh campaign



By midday on Friday, March 7th, Chimerix employees and Board members had already received hundreds of phone calls and emails in support of Josh.⁷

This included emails from friends of Chimerix employees and Chimerix

⁶ Aimee Hardy Caringbidge page. <http://www.caringbridge.org/visit/joshuahardy/journal/view/id/5319641ecb16b40c20fb0945>

⁷ Fredericksburg first-grader fighting for his life. Robyn Sidersky, Fredericksburg.com News Desk, March 7, 2014.

investors, as well as calls from politicians including a US Congressman and the Speaker of the Virginia House of Delegates.

Over the next two days, there was a barrage of statements on social media and within traditional media such as CNN, which ran an 8-minute segment on Josh Hardy and the family's request for brincidofovir. CNN's print headline was "Company denies drug to dying child." FoxNews carried the headline "Company Denies Drug to 7-Year-Old Boy Struggling Against Curable Virus,"⁸ ignoring the fact that brincidofovir was still in the experimental phase and thus the ability to "cure" an adenovirus infection was unproven.

On Monday March 10th, the #SaveJosh campaign trended in the top 5 on twitter, based in part on the participation of social media "amplifiers," individuals with large followings who retweeted the #SaveJosh message. By March 13th over 25,000 people had "liked" the Facebook page, which had been viewed by over 1.3 million people.⁹ The social media campaign was not only targeted at Chimerix's employees and board, but also at politicians and the FDA. Within these messages, a darker side of social media was exposed, one based on threats of violence.

⁸ Company Denies Drug to 7-Year-Old Boy Struggling Against Curable Virus. Fox News Insider, March 10, 2014. <http://foxnewsinsider.com/2014/03/10/drug-maker-chimerix-refuses-release-drug-7-year-old-josh-hardy-struggles-against-curable>

⁹ Facebook Savejosh – Posts March 7, 2017 to March 13, 2014.

<https://www.facebook.com/SaveJoshHardy/photos/a.666481530059683.1073741827.666476203393549/669181626456340/?type=1&theater>

In the face of this media storm, I tried to explain the ethical dilemma that Chimerix was facing, stating that “this is not only about Josh, it is about the many Joshes.”¹⁰ This approach did nothing to quell the uproar.

While the very public and highly negative social and traditional media frenzy pleading for access for Josh was ongoing, behind the scenes there were active conversations between Chimerix and the FDA about how to proceed, during which Chimerix maintained its position that for a multitude of reasons it did not have a clear path to make brincidofovir available to Josh Hardy under a single patient expanded access protocol. In response, the FDA proposed a novel solution. On Tuesday evening, March 11th, 120 hours after the first Facebook post by Mrs. Hardy, Chimerix announced in a press release that *“it has reached agreement with the FDA for the immediate initiation of a pilot trial of open-label brincidofovir for the treatment of adenovirus infections in immunocompromised patients.....This study is expected to begin with Josh Hardy as the first patient enrolled on Wednesday, March 12, 2014.”*¹¹

¹⁰ When unapproved drugs are the only help: A case for compassionate use. Jennifer Miller, Ethics Illustrated, August 18, 2014. <http://www.bioethics.net/2014/08/when-unapproved-drugs-are-the-only-help-a-case-for-compassionate-use/>

¹¹ Chimerix to Provide Brincidofovir to Josh Hardy as First Patient in New Open-Label Study in Patients With Adenovirus Infections, Chimerix Press Release, March 11, 2014. <http://ir.chimerix.com/news-releases/news-release-details/chimerix-provide-brincidofovir-josh-hardy-first-patient-new-open>

The ability to craft such a novel solution is rare, and would not have happened without the specific involvement of senior level FDA personnel.¹² As opposed to “conceding” in the face of social media pressure, the solution found was the initiation of a new Phase 3 clinical trial that in addition to treating Josh had the potential to provide data that could be used for the benefit of future patients who were faced with life threatening adenovirus infections– “the many future Joshes.”

I also want to take this opportunity to push back on the idea that the FDA is slow and ineffective with regard to expanded access, as is intimated in many “right to try” bills. The FDA approves more than 99 percent of these requests, on average, within four days¹³. For emergency requests, the agency responds in one day or less. The idea that these bills will give patients faster access to experimental drugs by cutting out the bureaucracy, which is a tenant in most of the Right to Try bills, is simply wrong. In reality, ending FDA oversight over experimental drugs would “expose the patients to exploitation without guaranteeing access to the drugs they seek. And weakening the FDA puts everyone else who takes drugs or uses medical devices or vaccines at grave risk.”¹⁴

¹² Chimerix Issues Statement Thanking the FDA for Collaboration in Developing Protocol to Treat Patients With Life-Threatening Adenovirus Infection, Chimerix Press Release, March 14, 2014. <http://ir.chimerix.com/news-releases/news-release-details/chimerix-issues-statement-thanking-fda-collaboration-developing>

¹³ “Expanded Access of Investigational Drugs: The Experience of the Center of Drug Evaluation and Research Over a 10-Year Period” Jonathan P. Jarow, Steven Lemery, MD, MHS, Kevin Bugin, MS, RAC, Sean Khozin, MD, MPH. Sage Journals, June 29, 2016

¹⁴ Expanded Access of Investigational Drugs: The Experience of the Center of Drug Evaluation and Research Over a 10-Year Period” Jonathan P. Jarow, Steven Lemery, MD, MHS, Kevin Bugin, MS, RAC, Sean Khozin, MD, MPH. Sage Journals, June 29, 2016

Josh Hardy received his first dose of brincidofovir on Wednesday night March 12th. His progress and response were reported by his mother through multiple Facebook posts¹⁵ and by March 31st, when Josh turned 8, adenovirus was undetectable.¹⁶ On April 10th, after fewer than 10 doses of brincidofovir and a month after his first dose, Josh was released from St. Jude, although he was required to remain in Memphis to be near his physicians.¹⁷ On July 17, he was allowed to return to his home in Virginia. Sadly, on September 22, 2016, 2 ½ years after receiving brincidofovir, Josh Hardy died of further complications of his underlying disease. He was 10 years old.

While brincidofovir provided Josh Hardy with additional time, many cases do not work out this way. And continuing to create policies that will encourage more patients to try and access unapproved drugs without FDA oversight, while well intentioned, is the wrong solution to such a serious issue. The laws will unlikely make a difference in the lives of patients, but will encourage this growing phenomenon of using social media to shame companies into providing access to unapproved drugs.

¹⁵ Aimee Hardy Facebook page. <https://www.facebook.com/aimee.hardy.5?fref=ts>

¹⁶ St. Jude Patient Celebrates Birthday And Improving Health, WREG Memphis, March 31, 2014. <http://wreg.com/2014/03/31/st-jude-patient-celebrates-birthday-and-improving-health/>

¹⁷ Josh Hardy released from hospital, Fredericksburg.com News Desk, April 11, 2014

The #SaveJosh social media campaign brought considerable publicity to expanded access and “right to try,” and much was written by bioethicists and others about the #SaveJosh social media campaign and its impact and implications for on expanded access, Right to Try and the development of experimental medicines. My learning experiences and observations will be more fully discussed in a soon to be published article in Medicine Access @ Point of Care entitled, “Ethical Crossroads: Expanded Access, Patient Advocacy and the #SaveJosh Social Media Campaign.”¹⁸

Hopefully, this expanded body of writings will provide more support and guidance to corporate leaders who are trying to make decisions about expanded access. However, at the time that Chimerix was faced with these questions very little had been written, and thus I relied on my own expanded access experiences at prior companies, on several Chimerix colleagues and on a number of industry leaders who had relevant experience in expanded access and crisis management, as well as on the “Statement of Ethical Principles on Early Access Programs” that had been published in 2010 by the Biotechnology Innovation Organization’s (BIO) Standing Committee on Bioethics.¹⁹

¹⁸ Ethical Crossroads: Expanded Access, Patient Advocacy and the #SaveJosh Social Media Campaign. Kenneth I. Moch, Under Revision, to be published in Medicine Access @ Point of Care, 2017. <http://medicine-access.pointofcarejournals.com/>

¹⁹ Early Access Programs: Points to Consider, Biotechnology Innovation Organization Standing Committee on Bioethics, April 16, 2010, <https://www.bio.org/sites/default/files/files/20100416.pdf>

Additionally, since the experience with Chimerix, considerable progress has been made on both the regulatory front by the FDA and in the legislative arena through the 21st Century Cures Act. 21st Century Cures now requires that all companies in the business of developing, manufacturing, and distributing drugs publish the policies and processes under which they will make their investigational unapproved medicines available to very sick patients. Importantly, they are required to provide a specific contact point where doctors can discuss the patient's need for the experimental medicine. It is policies like these that Congress should be focused on in continuing their work.

State and Federal legislators must be coming up with solutions that will ensure that all patients can get access to groundbreaking new treatments. Unfortunately, I believe that ultimately the potential confusion and complexities caused by states passing different variations of Right-to-Try laws will need to be addressed and corrected, which is another reason why I urge Congress to proceed with caution in this space. At its essence, expanded access is not drug development, and it cannot be used as an alternative to fully demonstrate the efficacy and safety of experimental medicines. The goal must not change – and that is to get a drug approved by the FDA so that it is available to be used in all appropriate patients.

There is no simple, monolithic answer to the question of when the circumstances and timing are right to undertake an expanded access program, because each experimental medicine is different, the safety and efficacy parameters are different, the clinical development processes and regulatory pathways are different, and the patient populations in need are different. Expanded access is not drug development and, given this fact, it is not unreasonable for a company to decide not to initiate an expanded access program until there is sufficient data demonstrating the efficacy and safety of an experimental medicine.

As I have noted, expanded access programs raise social, ethical and moral conflicts and dilemmas regarding access to experimental medicines. How does society or a company balance the immediate needs of a critically ill individual, in many cases a child, versus the potential needs of many future patients? Who is advocating for future patients who might not receive a needed medicine because FDA approval is delayed by even a week or a month?

I am not talking about the FDA delaying the review process, but rather what might happen if, because of an unexpected finding or outcome, some percentage of potential participants choose not to enroll in a clinical trial, slowing down its timeline. Being very granular, what would have happened

to the brincidofovir clinical development program and even to Chimerix if, after the global social media campaign, Josh Hardy had received brincidofovir and shortly thereafter died?

The ethical decisions should not rest solely on the corporate leadership in biotechnology companies. Instead, there needs to be a focused effort to create a more equitable approach to expanded access. In 2015, in a Wall Street Journal article, I laid out several proposals, some of which have already been adopted. ²⁰

- “Life-science companies should publicly state their policy on expanded access. It must be recognized that a company has the right not to make an experimental medicine available if it believes the greater good is served by this decision.”

This was actually a proposal adopted in 21st Century Cures, which I applaud.

- “Regulatory guidance should provide a framework so companies can consider the risks to the drug development timeline and approval

²⁰ Wanted: Guidelines for Access to Experimental Drugs, Kenneth Moch, The Wall Street Journal, March 16, 2015. <https://www.wsj.com/articles/kenneth-i-moch-wanted-guidelines-for-access-to-experimental-drugs-1426547602>

pathway in the face of unforeseen or unfortunate consequences from granting expanded access.”

While the FDA has done a great deal to provide guidance, there needs to be a greater partnership and coordination with the agency.

- “Especially for smaller companies whose drug or device may be their only product, there should be an optional system to provide support for these complex decisions that would look at multiple factors, including equitable access and availability, cost, and the short- or long-term risks and benefits to a development program.”

Complex situations are often best analyzed in hindsight. Now, over 3 ½ years after the #SaveJosh social media campaign, it is clear to me that I would not change any of the key decisions that I made in dealing with the external forces and interests.

Key learning experiences stand out. First, despite all the hope and desire, not all experimental medicines succeed in clinical testing. Brincidofovir did not achieve the level of effectiveness in either of its two Phase 3 clinical trials, and the company has had to reposition its development efforts for the compound to progress towards regulatory approval. This highlights one of

the underlying complexities of the use of experimental medicines, as stated above: expanded access is not drug development. While there is evidence of a high approval rate for drugs provided under expanded access²¹, the understanding of safety and efficacy of an experimental medicine is still evolving, and there are no guarantees that the experimental medicine will have the desired effect without undesired side effects. For growing biotech companies with voracious capital requirements, successful market structure reform would lead to scientific advancement, novel medicines, and life-saving treatments for patients in need.

Also, as I mentioned earlier, the FDA is not an impediment in patients getting access to experimental medicine. Rather, they are a necessary partner and must be engaged in the process as a partner with the company, for the safety of all patients.

Finally, social media cannot and must not drive these decisions. The social media uproar regarding Josh Hardy exploded and reached a conclusion over the course of five days, just 120 hours, and as a result, there was much analysis over the power of social media in influencing the decision-making process regarding access to health care. On March 23, The Washington Post published an article entitled, "Crowdsourcing medical decisions: Ethicists

²¹ Characterizing expanded access and compassionate use programs for experimental drugs, Miller et al, BMC Res Notes, July 28, 2017. <https://www.ncbi.nlm.nih.gov/pubmed/28754150>

worry Josh Hardy case may set bad precedent” in which the author noted that “critics of the strategy say they sympathize with Josh’s parents and admire them for being willing to do anything to save their child, but they decry the crowdsourcing of medical decisions and warn that the case may set a dangerous precedent.”²²

I know firsthand that collective public opinion marshalled by social media can create immediate pressure which is difficult if not impossible to ignore. And these new laws are encouraging and rewarding these actions, resulting in individual companies being forced to make decisions on an ad hoc basis, which will only continue to fuel suspicions among patients, family members and the public about the motives when access is denied.”²³ The climate of innovation needs to be fostered, not vilified. These growing biotech companies are trying to drive scientific advancement, and bring novel medicines and life-saving treatments for ALL patients in need.

I do not want to end this testimony without providing a concept for consideration, a potential way to work with and embrace the intent of Right to Try legislation.

²² Crowdsourcing medical decisions: Ethicists worry Josh Hardy case may set bad precedent. Ariana Eunjung Cha, The Washington Post, March 23, 2014. https://www.washingtonpost.com/national/health-science/crowdsourcing-medical-decisions-ethicists-worry-josh-hardy-case-may-set-bad-precedent/2014/03/23/f8591446-ab81-11e3-adbc-888c8010c799_story.html

²³ Viral Crossroads, Steve Usdin, BioCentury, March 31, 2014. <https://www.biocentury.com/biocentury/regulation/2014-03-31/hardy-case-shows-flaws-compassionate-use-system-provides-catalyst>

One way to meld the intent of Right to Try laws with the existing expanded access process would be to create a more explicit regulatory pathway which allows expanded access safety and efficacy data to be incorporated into the label of a new medicine once it is formally approved for its primary indication via “traditional” placebo controlled trials. In this way, companies could balance the risks and benefit to individual patients with the needs of future patients.

Under current expanded access regulations and Right to Try legislation, safety and efficacy data gained through expanded access programs is viewed as uncontrolled data that can provide only limited support to the drug development and approval process. As demand for expanded access increases, the lack of specific incentives to offset the costs and risks can and most likely will become a factor in the decision to allow expanded access, a decision that, as noted, rests primarily with the sponsor companies.

This might require legislative and/or regulatory changes to existing guidelines for intermediate- or large-scale expanded access programs.

Rather than circumventing the FDA oversight process, companies would have to reach agreement with the FDA as to the parameters under which “real-world evidence” collected from patients enrolled in these larger-scale expanded access trials could be used to support additional label claims for a new medicine. These programs would be “open label” trials, conducted

without placebo controls, but overseen as if they were formal clinical trials designed to provide full input into the drug development process.

Such programs would also have the benefit of obviating the need for incremental funding from third parties, unlike an oft-proposed national pool from which drug development companies would be paid for the cost of providing experimental medicines and managing Right to Try programs.

Under this amended expanded access proposal, companies would be incented to undertake these programs because they could determine how the expanded access program would potentially lead to the ability to treat a larger future patient population.

All of us who are committed to creating life-saving medicines would like to see our medicines made available to as many people as possible as quickly as possible. In order for that to happen, we need to conduct rigorous clinical trials so that both the efficacy and safety are well understood by doctors and their patients. However, we also recognize that this drug development process is lengthy and complex, and that there are patients in need now who cannot wait for the approval process to be completed. Rather than skirting regulatory oversight through Right to Try legislation, creating the potential for label claims which build on the data from larger expanded access programs may save their lives.

Thank you again for allowing me the opportunity to testify today.