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June 12, 2020

The Honorable Diana DeGette  
United States House of Representatives  
2111 Rayburn House Office Building  
Washington, DC 20515

The Honorable Fred Upton  
United States House of Representatives  
2183 Rayburn House Office Building  
Washington, DC 20515

**RE: Comments on 21<sup>st</sup> Century Cures 2.0 Concept Paper**

Dear Representatives DeGette and Upton,

The Institute for Gene Therapies (IGT or “the Institute”) is grateful for the opportunity to provide comments on the 21<sup>st</sup> Century Cures 2.0 Concept Paper and supports Congress’ efforts to realize the value of transformative therapies for patients, caregivers, the healthcare system, and society. The 21st Century Cures Act has helped to advance medical research and foster a new era of medical innovations that may ultimately establish new cures for the world’s most devastating diseases. Efforts to develop the “Cures 2.0” package continue that legacy, including a number of policies that would be beneficial to the work of the federal government in response to the current pandemic.

IGT was launched in February of 2020, with a focus on advocating for a modernized regulatory and reimbursement framework that encourages the development of transformative gene therapies and promotes patient access. IGT aims to inform the conversation regarding the value of transformative therapies and advocate for policies and practices that can ensure this value is realized to improve the lives of patients with rare diseases. Our comments focus on Title VI: Centers for Medicare and Medicaid Services (CMS) Modernization, Title V: Food and Drug Administration (FDA), and Title VII: Technical Provisions of the Concept Paper, with a specific goal of encouraging patient access to gene therapy and genetic disease screening, as well as establishing modernized reimbursement pathways.

**I. TITLE VI: CMS Modernization**

The looming necessity for the federal government to take action to modernize reimbursement systems for gene therapies increases in significance each year: FDA has prioritized the acceleration of gene and cell therapy approvals and expects to receive over 200 investigational new drug applications (INDs) per year, adding to the 800 active gene and cell-based therapies currently on file.<sup>1</sup> By 2025, FDA anticipates that the agency will be

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<sup>1</sup> *Statement from FDA Commissioner Scott Gottlieb, M.D. and Peter Marks, M.D., Ph.D., Director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies*, FOOD & DRUG ADMIN. (Jan. 2019),

approving 10 to 20 cell and gene therapy products per year.<sup>2</sup> The development of a reimbursement system equipped to adequately reimburse providers for administering these groundbreaking innovations will only grow in importance as the advancement of biotechnology pipelines results in increasingly specialized treatment into rarer diseases.

This section of IGT's comments responds to Congress' request for feedback on questions relevant to coverage reform for redefining care access and delivery and CMS Modernization for gene therapies, including the following sections of the Cures 2.0 Concept Paper: General Coverage Modernization; Cell and Gene Therapies; Medical Products for Small Patient Populations; Genomic Sequencing; and Breakthrough Coverage.

### **A. General Coverage Modernization**

Current coverage and reimbursement rules for innovative gene therapies under federal healthcare programs are desperately in need of reform. Federal healthcare program reimbursement mechanisms were not designed with potentially curative, short-course therapies in mind. For such therapies, regulatory barriers such as the federal Anti-kickback Statute (AKS), price reporting methodologies, FDA manufacturer communications guidelines, and HIPAA privacy protections limit full-scale, outcomes-based payment arrangements in both the government and private markets. While the need for modernization of these systems has become acutely apparent now that gene therapies are available on the market in the United States (U.S.), this need will become more severe as the advancement of biotechnology pipelines result in increasingly specialized treatments into rare diseases and the number of therapies available continues to grow. IGT encourages Congress to take action through Cures 2.0 to revise traditional payer parameters that were not designed for one-time therapies.

- **Federal Healthcare Program Price Reporting Revisions**

For a drug or biologic to be payable under Medicaid and Medicare Part B, Section 1927 of the Social Security Act (SSA) requires manufacturers to agree to participate in the Medicaid Drug Rebate Program, the 340B Pharmaceutical Pricing Program, and execute agreements with Department of Veterans Affairs for listing products on the Federal Supply Schedule. Through participation in these programs, manufacturers are required to provide mandatory rebates or offer drugs at established ceiling prices, as well as submit extensive price reporting data to the government as specified by the program. These price reporting methodologies, many of which are based on "per unit" utilization data and computations, were established long before potentially curative, one-time therapies were envisaged in the U.S. While manufacturers of gene therapies coming to the market today must attempt to apply these methodologies to their therapies, these systems are ill-equipped to support a future landscape of one-time therapies, particularly when outcomes-based payment models are considered.

Under an ideal, modernized system, IGT recommends development of a wholly new price reporting approach specific to gene therapies, including those administered under value-based payment arrangements (VBAs), rather than attempting to fit gene therapies into a system built primarily for chronic therapies and "per unit" methodology calculations. This type of system would provide mechanisms for calculating and providing payment of the financial obligations applicable for a product under relevant mandatory discount, rebate, and ceiling price requirements in federal healthcare programs, without otherwise attempting to apply methodologies that are ill-suited to potentially curative therapies. IGT emphasizes that State Medicaid Programs would still receive the

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<https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics>.

<sup>2</sup> *Id.*

standard Medicaid drug rebate and any inflationary rebate, if applicable, and related obligations to the 340B Program and other federal programs would be fulfilled, but the system would be better tailored to reporting data for one-time therapies, including under potential VBAs.

To the extent these types of wide-ranging revisions are not undertaken, Congress should institute amendments to the regulatory definitions of price reporting metrics that pose barriers for VBAs, such as Medicaid Best Price, Average Manufacturer Price (AMP), and unit price, as well as Medicare Part B Average Sales Price (ASP), to define the terms for payments made pursuant to VBAs. Congress should encourage the Department of Health and Human Services (HHS) to provide clarifying guidance on how manufacturers can incorporate VBAs into their price reporting calculations and provide necessary waivers and exclusions for rebates and price reductions tied to outcomes-based payment metrics. These waivers and exclusions would apply to rebates greater than the standard, mandatory rebate, as highlighted in the preceding paragraph.

- **Addressing Disparate Reimbursement Methodologies Across Settings of Care**

Provider and patient access to transformative therapies varies based on setting of care in payer programs due to the bundled versus separate payment methodologies that apply in the setting where the therapy is administered. For example, under Medicare Part B, the outpatient prospective payment system currently reimburses for transformative therapies administered in the hospital outpatient department at a rate of the ASP plus six percent for separately payable therapies, with availability of Transitional Pass-through Payment Status to ensure separate payment at ASP plus six percent for three years for new therapies that might otherwise be packaged into payment with the administration procedure or paid at a lesser rate. This separate payment for outpatient gene therapies enhances access for providers and patients and offers clarity regarding reimbursement.

Under Medicare Part A, however, the inpatient prospective payment system provides reimbursement for transformative therapies administered in the hospital inpatient setting based on the diagnostic-related group (DRG), which results in a lump sum reimbursement for all care a patient receives during a stay. In Medicare, New Technology Add-on Payments (NTAP) are available for eligible transformative therapies, which assists in facilitating access for providers in the first few years following launch. Separate payment for a transformative therapy in Medicare is not available in this setting, potentially placing financial burdens on providers.

These discrepancies between reimbursement based on setting of care are even more acute in Medicaid, where add-on payment mechanisms for new and innovative therapies are not available. This dynamic is of critical importance, as Medicaid will be a significant payer for gene therapies based on the goal of treating many genetic diseases as early as possible in childhood and the large proportion of children in America receiving healthcare coverage through Medicaid. Cures 2.0 should contemplate how Medicaid payment for inpatient services differs significantly from state-to-state due to the different payment methodologies employed, such as diagnosis-related groups (DRGs), *per diem*, and on a cost-basis. States establish reimbursement rates which may be inadequate to cover the cost of new innovations, such as gene therapies, and no add-on payment mechanisms, such as NTAP, exist in Medicaid.

Several states, however, have begun “carving out” these transformative therapies from the inpatient payment bundle and requiring providers to bill for them as separately payable outpatient therapies. For example, Massachusetts and New York have created carve-out programs for CAR T-cell therapies from both inpatient and outpatient bundled payment mechanisms to be paid separately. States generally are required to seek CMS approval prior to implementing these carve-outs. IGT encourages Congress to mandate issuance of federal guidance from CMS to State Medicaid Directors to provide blanket approval for enabling carve-outs, which

would offer greater flexibilities to states seeking to follow the same approach. Such guidance would reduce the burden to states for participating in such arrangements by eliminating the need for states to engage in one-off agreements, or to seek approval individually.

- **Modernized Compliance Rules**

Fraud and abuse laws, regulations, and guidance also have not kept pace with the advent of gene therapy and stakeholder interest in VBA development. IGT encourages Congress to require HHS to establish a new safe harbor to the Federal Anti-kickback Statute for protecting VBAs for transformative therapies or issue clarifications for using existing safe harbors. Congress should also address other fraud and abuse concerns presented by laws such as the False Claims Act, Stark Law, and Beneficiary Inducements Statute to provide clear pathways for advancement of VBAs and reduce the burden on the Office of the Inspector General for addressing individual manufacturer requests for advisory opinions and guidance.

## **B. Cell and Gene Therapies**

The true value of cell and gene therapies lies in their potential to confer a transformative, durable effect in a short treatment course. For instance, a hemophilia A patient's lifetime costs can amount to over \$20 million, whereas a gene therapy can help not only potentially treat the patient, but reduce many of the associated life time costs and burdens of current chronic care options.<sup>3</sup> Transformative therapies can not only save but also enhance the quality of life for individuals afflicted by rare genetic diseases. Without proper reimbursement mechanisms, however, the ability of transformative therapies to achieve wide-ranging uptake is limited. IGT urges Congress to use Cures 2.0 to establish a clear legal pathway for manufacturers to offer VBAs in a compliant and voluntary manner across all payers, both public and private.

Development of this pathway is imperative for modernizing the U.S. reimbursement system to focus on value and outcomes in a manner that is cognizant of the unique nature of potentially curative therapies and away from using systems developed for chronic disease treatments. This type of pathway would provide clarity to all parties regarding the overarching compliance, price reporting, and reimbursement laws and regulations that apply to VBAs and provide flexibility to manufacturers and payers in tailoring VBAs individually for the applicable gene therapy. For example, a clear pathway would permit flexibility for providers to compliantly waive patient cost-sharing or permit manufacturers to cover travel and lodging costs of patients, as well as enabling carve outs of gene therapy reimbursement from bundled payment mechanisms to facilitate a VBA and permitting alternative payment models, such as annuity or payment over time structures. It would streamline processes for developing and executing VBAs without overly burdensome administrative processes and extensive uncertainty regarding legal and compliance issues. While manufacturers and payers have expressed great interest in engaging in VBAs, the lack of this type of clear pathway and mechanisms for offering multi-payer arrangements has significantly hampered forward progress.

IGT seeks action on the part of Congress in part to ameliorate the burden on states and CMS to use existing waiver authorities, and to support the agency's efforts to clarify use of such authorities. Over the last two years, CMS has engaged in dialogue exploring approaches to facilitate innovative payment arrangements and has noticed a number of forthcoming proposed rules and guidances

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<sup>3</sup> Joshua T. Cohen et al., *Putting the Costs and Benefits of New Gene Therapies into Perspective*, HEALTH AFFAIRS (Sep. 4, 2019), <https://www.healthaffairs.org/doi/10.1377/hblog20190827.553404/full/>.

on the topic.<sup>4</sup> However, to-date such guidances and proposed rules have not been executed and no such innovative payment arrangement for one-time therapies has been approved through waiver authority or by the Center for Medicare and Medicaid Innovation (CMMI). Furthermore, CMS clarified in its CY 2020 Hospital Outpatient Prospective Payment System Final Rule that revising or creating a new payment pathway for gene and cell therapies is outside the scope of CMS authority. In the absence of CMS using its existing regulatory authority to implement innovative payment arrangements for gene and cell therapies, IGT urges Congress to develop a novel reimbursement pathway to drive sustainability for transformative therapies, while enabling patient access and appropriate provider payment.

### **C. Medical Products for Small Populations**

Several significant impediments exist to new cures development for therapies intended to benefit small populations. Gene therapies may be approved by FDA based on smaller trials, novel endpoints, and trial designs, as well as expedited regulatory mechanisms. Large, randomized placebo-controlled trials are not the norm for transformative therapies and, thus, evidence derived from smaller-scale trials and novel designs should be viewed differently. IGT seeks action on the part of Congress to ward against payers using these smaller trials as rationale for setting coverage policies that are narrower than the FDA-approved label. The Institute also encourage Congress to use Cures 2.0 as a vehicle for supporting the sustainability and growth of genetic testing coverage, both through universal Newborn Screening (NBS) and screening for children and adults for genetic disorders/disease for which treatments become available after NBS administration.

- **Aligning Coverage with FDA-labeled Indications**

Based on the heterogeneous nature of many rare diseases, it is extremely challenging to include patients in trials that span the entire spectrum of the disease state. FDA has demonstrated recognition of these challenges and considers scientific plausibility, mechanism of action, and other factors in determining whether the potential benefits outweigh the potential risks across a broader population than may have been included in trials. Unfortunately, payers often implement coverage policies that do not align with the FDA-approved label. Reinforcing coverage to align with the FDA-approved label, as is already required by the Medicaid Drug Rebate Program Statute (SSA Section 1927), would deter payers from restricting access by imposing coverage criteria that inappropriately mirror the clinical trial criteria. More specifically, IGT urges Congress to mandate that CMS release guidance to states requiring issuance of a Medicaid fee-for-service policy for transformative therapies to reiterate state obligations to cover “covered outpatient drugs” of a manufacturer participating in the Medicaid Drug Rebate Program and enforcing adherence to this same coverage for Medicaid managed care organizations (MCOs). IGT is concerned that MCOs are following more restrictive coverage policies, leading to disparities in care and access within a state Medicaid program.

In addition, Congress should require CMS to issue guidance to state Medicaid agencies to require them to modernize their review of manufacturer data to facilitate immediate patient access upon FDA-approval.

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<sup>4</sup> For example, the 2019 Unified Agenda highlighted a proposed rule under consideration on CMS Medicare Coverage of Innovative Technologies. CMS highlighted that this proposed rule would streamline the Medicare coverage process for breakthrough technologies that have “the potential to improve patient health outcomes and quality of care.” The time frame for release was listed as December 2019, but it has not yet been disseminated. Similarly, the 2019 Unified Agenda included a CMS proposed rule titled “Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value Based Payments (VBP) for Drugs Covered in Medicaid.” CMS stated that this proposed rule would include modifications to the Medicaid Drug Rebate Program (MDRP) regulations to enable VBP arrangements between states and manufacturers. This rule has not yet been released, but OMB announced that it had completed its review of this proposed rule on June 9, 2020.

Coverage in Medicaid is required immediately upon approval for new drugs of a manufacturer with a rebate agreement, including for Medicaid MCOs.<sup>5</sup>

- **Expediting Code Creation and Uptake for Transformative Therapies**

The Breakthrough Therapy, regenerative medicine advanced therapy (RMAT), and Accelerated Approval pathways are critical for facilitating priority review of transformative therapies; however, following FDA-approval, patients and providers may face claims processing hurdles due to the lack of an ICD-10 diagnosis code for these rare diseases. Inaccurate coding often leads to providers engaging in time-consuming appeals and exceptions processes to demonstrate a patient’s diagnosis to payers. Thus, a lack of diagnosis coding can hinder patient access to transformative therapies, which significantly impacts patients suffering from rare, progressive, and oftentimes fatal, genetic diseases.

Cures 2.0 should also consider requiring CMS to implement expedited product code processes for innovative, transformative therapies to make unique codes available closer in time with commercialization. As explored by a previous iteration of the CARES Act, such expedited coding procedures would be associated with Breakthrough, RMAT, and Accelerated Approval designations and linked to an accelerated coding implementation timeline. For example, a quarterly Healthcare Common Procedure Coding System (HCPCS) process would reduce the time to granting of a code by 50 percent, even under the newly created expedited process, where a six-month gap exists between the time of requesting a code and the code effective date. Another example of enhanced coding could be creating a requirement for a code modifier for inpatient hospital services in Medicare to “track utilization and outcomes of novel medical products.” This modifier could potentially assist in removing steps in the New Technology Add-on Payment (NTAP) process for manufacturers, to the extent it serves as a proxy for obtaining an ICD-10 procedural code for new technology.

- **Bolstering Screening for Genetic Diseases**

Rare disease patients, as well as their families and caretakers, face significant challenges in receiving conclusive diagnoses. With over 6,000 rare diseases, 72 percent are genetic and 70 percent of those genetic diseases begin in childhood.<sup>6</sup> These rare, genetic diseases have a variety of signs and symptoms that manifest differently in patients, resulting in misdiagnoses and delayed treatment. Furthermore, delayed treatment and misdiagnoses result in severe decreases in quality of life due to the debilitating nature of such diseases, which often cause chronic, degenerative, progressive, and life-threatening issues. Without accessible screening for such conditions, an unnecessary increase in morbidity and mortality may occur for patients with rare diseases.

To mitigate unnecessary misdiagnoses, optimize outcomes, and accelerate new cures development, newborn screening (NBS) and genetic testing must be modernized. Enhanced access is needed to screening tests that can facilitate diagnosis, monitoring, and treatment, which are all critical for patients with rare and serious diseases. Availability and affordability of genetic testing is key to ensuring that patients are aware of clinical studies and can obtain the benefits of approved gene therapies. Robust genetic screening should be available to newborns, and all people at elevated risk or suspected of having a genetic disorder. All payers in U.S., including public and private insurers, should establish policies for automatic coverage of the appropriate genetic tests at the time of approving coverage for a new gene therapy for a genetic disease/disorder in order to prevent undue treatment delays.

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<sup>5</sup> 81 Fed. Reg. 27498, 27551 (May 6, 2016).

<sup>6</sup> *Key Figures*, RARE DISEASE DAY (2020), <https://www.rarediseaseday.org/article/what-is-a-rare-disease>.

At the federal level, the Advisory Committee on Heritable Disorders in Newborn and Children (ACHDNC) is responsible for recommending disorders for newborn screening. The Committee includes representatives from across HHS, as well as a variety of healthcare experts. The ACHDNC maintains a Recommended Uniform Screening Panel (RUSP), which consists of a standardized list of disorders that are recommended for states to implement in their NBS programs. The Committee engages in lengthy processes for evaluating the disorders to include on the list. While the majority of states screen for most disorders on the list, some states screen for additional disorders and others are at various stages of adopting more recent recommendations. State public health departments are tasked with making determinations on the tests to include within the state NBS program, resulting in a lack of consistency across states. Support and funding for these programs at the state and federal levels is critically important for ensuring their sustainability and broadening their reach in the future to include a wider range of genetic diseases.

IGT encourages Congress to reauthorize the Newborn Screening Saves Lives Act, which expired in September of 2019, and provides vital funding for continuing the program. Furthermore, we urge Congress to consider opportunities to ensure the entire U.S. newborn screening ecosystem, including the federal RUSP process and states, can keep pace with transformative new technologies, which could include:

- public-private partnerships for financing newborn screening pilots and implementation of new conditions;
- modernization of the RUSP process to eliminate redundancies and accelerate the ability to recommend new conditions, including preliminary RUSP inclusion/or RUSP expansion for conditions with gene therapies in development or that received marketing approval; and,
- additional funding and support to states to accelerate state compliance with RUSP recommendations.

#### **D. Breakthrough Coverage**

As expanded upon in the Section II B, Cures 2.0 can address barriers to coverage of transformative therapies approved through FDA's breakthrough and accelerated approval pathways.

## **II. Title V: FDA**

### **A. Increasing Use of Real-World Data/Evidence**

Cures 2.0 "builds on FDA's efforts by (1) requiring guidance on utilizing real-world evidence (RWE) in Breakthrough Therapy and Accelerated Approval drugs; (2) requiring HHS to establish a consistent framework for RWE; and (3) establishing a task force to develop recommendations on ways to encourage patients to engage in real-world data generation." IGT is supportive of this proposal. RWE has already shown significant benefit in the post-market setting for providing additional data that support continued access and to satisfy post-marketing requirements. These RWE post-marketing benefits are especially significant for gene therapies due to the challenges of gathering post-market evidence due to the small, heterogeneous patient populations these treatments target.

### **B. Improve FDA-CMS Communication regarding Transformative New Therapies**

Congress is seeking feedback on a proposal to establish an automatic communication requirement between FDA and CMS for products granted Breakthrough Therapy designation. The communication requirement would

commence upon the grant of the designation and would continue through the collection of any RWE post-FDA approval.

While IGT supports removing barriers which facilitate immediate patient access to transformative gene therapies upon FDA approval, it cautions that mandating such broad communication or coordination may not have the intended effect of facilitating expedited access and may instead increase the burden on FDA and could delay approval and access of much needed therapies. In federal healthcare programs, such as Medicare and Medicaid, parameters exist to enable coding, coverage, and payment at launch for transformative therapies that satisfy statutory criteria. Moreover, there is little data the FDA could share with CMS that the sponsor could not provide directly, with the potential for additional burdens on review staff. Such communication could result in increased utilization of restrictive coverage policies upon launch or use of Coverage with Evidence Development (CED) policies that curtail access rather than expedite it.

However, IGT does believe that some communication between FDA and CMS, specifically for the purposes of expedited code creation by CMS, would provide more timely access to products granted with either Breakthrough Therapy or regenerative medicine advanced therapy (RMAT) designations or through the Accelerated Approval pathway. This would allow for CMS to expedite work on relevant coding processes that facilitate reimbursement and claims processing when a new treatment is approved, which in turn would streamline uptake of new therapies upon approval. For example, there is approximately a one- to two-year lag between ICD-10-CM diagnosis code introduction and implementation. This timeline is set by statute, resulting in a very structured, but innately slow procedure for updating clinical and procedural codes. As discussed above, Cures 2.0 should accelerate the timeline for establishing new diagnosis codes for disorders treated by innovative, transformative therapies.

We look forward to working more on this issue to enhance timely access to transformative therapies using well-structured communication between FDA and CMS pertaining to coding.

### **III. Title VII: Technical Provisions**

Congress authorized the fast track, breakthrough therapy, and RMAT designation programs at FDA with the goal of expediting the development and review of drugs that preliminary clinical evidence indicates could benefit patients living with serious or life-threatening diseases or conditions. Specifically, under the Federal Food, Drug, and Cosmetic Act (FFDCA), fast track designation is granted if the drug “demonstrates the potential to address unmet medical needs for [a serious disease or condition],”<sup>7</sup> breakthrough designation is granted if “preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints,”<sup>8</sup> and RMAT designation is granted when “preliminary evidence indicates that the drug has the potential to address unmet medical needs for [a serious or life-threatening] disease or condition.”<sup>9</sup> Each of these designations afford a drug sponsor increased interaction with FDA and is intended to expedite the development of the drug and review of the application.

The preliminary clinical evidence included in such designation requests is generally collected during relatively small trials conducted in the U.S. In order for a drug sponsor to test an investigational drug in humans in the U.S., they must have an active IND application in place. However, an IND is not required if the clinical (human) studies solely occur in other countries. As FDA acknowledged several years ago, “Clinical research is becoming

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<sup>7</sup> See 21 U.S.C. § 356(b)(1).

<sup>8</sup> See 21 U.S.C. § 356(a)(2).

<sup>9</sup> See 21 U.S.C. § 356(g)(3).

increasingly global . . . Sponsors may decide to use the data that is obtained from non-IND foreign sites to support clinical investigations and/or marketing approval(s) in the [U.S.]. Some sponsors may even seek to rely solely on foreign clinical data as support for an IND or application for marketing approval in the U.S. Indeed, the number of INDs and applications for marketing approval supported by foreign clinical trials has increased in recent years and will likely continue to increase in the future.”<sup>10</sup> This is particularly true in the case of rare diseases with extremely small patient populations not conveniently clustered around U.S.-based treatment centers.

For example, the amyotrophic lateral sclerosis (ALS) drug edaravone was approved in 2017 utilizing data from a six-month study in Japan. The sponsor of the drug did not submit an IND, per FDA’s request: “After learning about the use of edaravone to treat ALS in Japan, we rapidly engaged with the drug developer about filing a marketing application in the [U.S.],” said Eric Bastings, M.D., deputy director of the Division of Neurology Products in the FDA’s Center for Drug Evaluation and Research.<sup>11</sup> This type of agency action should be encouraged as more drugs are approved using similar data cohorts, but this should not preclude a drug from the benefits of FDA’s various accelerated approval programs.

While a sponsor may choose not to submit an IND for these legitimate reasons, the Fast Track, Breakthrough, and RMAT provisions in the FDCA do not contemplate a scenario where a designation request would be made based on preliminary clinical evidence solely collected outside of the U.S., prior to or absent the submission of an IND. Specifically, sections 506(b)(1), 506(a)(2), and 506(g)(3) state that such requests may be made “concurrently with, or at any time after, the submission of an [IND]” and FDA has taken the position that it will only review designation requests if there is an active IND in place. Filing an IND is not a perfunctory matter, nor should it be viewed as an administrative means to an end, as it must include the design, institutional review, and approval of a clinical trial protocol. Therefore, Congress should remedy this unforeseen impediment to sponsors which have collected scientifically valid preliminary clinical evidence outside of the U.S. to receive the benefits of these designations for investigational drugs that otherwise meet the qualifying criteria.

### **Hypothetical Case Study**

A sponsor is conducting an open-label trial at a reputable site in Europe for an investigational gene therapy on patients with an ultra-rare disease. The preliminary clinical evidence is rigorously collected, and the results are extremely compelling in patients who have no other options. FDA indicates that the sponsor should apply for marketing approval and not wait for additional clinical testing to be conducted in the U.S. Accordingly, the sponsor does not move forward with an IND and cannot, therefore, receive Fast Track, Breakthrough, or RMAT designation and the resulting benefits.

### **Potential Legislative Approach**

#### ***FAST TRACK DESIGNATION***

##### **Section 506(b)(2)**

The sponsor of a new drug may request the Secretary to designate the drug as a fast track product. A request for the designation may be made **at any point before submission of an application for approval of the drug under section 355(b) of this title or licensure under section 351(a)(2) of the Public Health**

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<sup>10</sup> *Guidance for Industry and FDA Staff: FDA Acceptance of Foreign Clinical Studies Not Conducted under an IND Frequently Asked Questions*, 2 U.S. FOOD AND DRUG ADMIN., <https://www.fda.gov/media/83209/download>.

<sup>11</sup> *FDA Approves Drug to Treat ALS*, U.S. FOOD AND DRUG ADMIN., (May 2017), <https://www.fda.gov/news-events/press-announcements/fda-approves-drug-treat-als>.

**Service Act [42 U.S.C. 262(a)(2)]** concurrently with, or at any time after, submission of an application for the investigation of the drug under section 505(i) or section 351(a)(3) of the Public Health Service Act. —

***BREAKTHROUGH DESIGNATION***

**Section 506(a)(2)**

The sponsor of a drug may request the Secretary to designate the drug as a breakthrough therapy. A request for the designation may be made **at any point before submission of an application for approval of the drug under section 355(b) of this title or licensure under section 351(a)(2) of the Public Health Service Act [42 U.S.C. 262(a)(2)]** concurrently with, or at any time after, the submission of an application for the investigation of the drug under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

***REGENERATIVE MEDICINE ADVANCED THERAPY DESIGNATION***

**Section 506(g)(3)**

The sponsor of a drug may request the Secretary to designate the drug as a regenerative advanced therapy **at any point before submission of an application for approval of the drug under section 355(b) of this title or licensure under section 351(a)(2) of the Public Health Service Act [42 U.S.C. 262(a)(2)]** concurrently with, or at any time after, submission of an application for the investigation of the drug under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

**Conclusion**

IGT appreciates the opportunity to provide input on the 21<sup>st</sup> Century Cures 2.0 Concept Paper and looks forward to the opportunity to engage with Congress as this effort moves forward. The Institute supports developing a sustainable, flexible, and permanent payment pathway that modernizes regulatory parameters and is reflective of the advances in science resulting in such transformative therapies. IGT would be pleased to serve as a resource on gene therapy issues during this process and answer any questions regarding these comments.

Sincerely,



The Honorable Erik Paulsen  
Chairman  
Institute for Gene Therapies