



# Alliance *for* Regenerative Medicine

December 16, 2019

The Honorable Diane DeGette  
2111 Rayburn House Office Building  
Washington, DC 20515

The Honorable Fred Upton  
2183 Rayburn House Office Building  
Washington, DC 20515

(Sent via [cures2@mail.house.gov](mailto:cures2@mail.house.gov))

Dear Representatives DeGette and Upton:

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to respond to your request for input as you consider a “Cures 2.0” initiative.

ARM is an international multi-stakeholder advocacy organization that promotes legislative, regulatory, and reimbursement initiatives necessary to facilitate access to life-giving advances in regenerative medicine worldwide. ARM comprises more than 350 leading life sciences companies, patient groups, research institutions and investors that represent the regenerative medicine and advanced therapies community. ARM takes the lead on the sector’s most pressing and significant issues, fostering research, development, investment, and commercialization of transformational treatments and cures for patients worldwide. The majority of regenerative medicine therapies developed by ARM members focus on rare or orphan diseases that often lack other clinically effective treatment options.

Prior to providing our initial recommendations for inclusion in Cures 2.0, ARM wanted to take this opportunity to again thank you for your leadership in navigating the “21<sup>st</sup> Century Cures Act of 2016” through the legislative process and to enactment. We are particularly pleased that this landmark legislation created the Regenerative Medicine Advanced Therapy (RMAT) designation. To date, there have been over 100 requests for RMAT designation by therapy developers, and forty-four have been granted. Additionally, the legislation also resulted in the creation of the Standards Coordinating Body for Gene, Cell, and Regenerative Medicine and Cell-Based Drug Discovery (SCB) whose mission is to “coordinate the accelerated advancement and improved awareness of the standards and best practices that address the rapidly evolving needs of the global regenerative medicine advanced therapy community.” The SCB has already taken significant steps to facilitate development and use of standards in the sector.

As you have noted, despite the success of the 21<sup>st</sup> Century Cures Act, “there is more work to do.” ARM strongly agrees with you and is pleased to share our recommendations as to topics that need further attention.

### **Remove Barriers to Adoption of Alternative Payment Models**

Today, our health care system generally operates in a fee-for-service (FFS) construct in which payment is based on volume and level of services provided. Unfortunately, this methodology does not work for regenerative medicine therapies (treatments intended to repair or replace damaged cells, tissues, or organs that are often delivered in a single administration, and have long-term durability and are potentially curative). ARM agrees with Department of Health and Human Services Deputy Secretary Eric D. Hargan when he noted that the current FFS approach “does not necessarily translate to the modern health care system.”<sup>1</sup>

Value-based arrangements serve to link payments to performance in ways that account for both the cost and quality of care provided. The most basic value-based purchasing model may function essentially as an obligation to refund all or part of the payment if it did not meet certain agreed upon levels of efficacy for a particular patient or group of patients. One variation to this model is to finance the cost of treatment over time through an initial or discounted payment when the therapy is administered, with future payments for the remaining cost of the treatment contingent upon meeting certain defined clinical outcomes or other measures at fixed intervals over a period of time. Both of these options present significant benefits when such treatments otherwise require a higher upfront investment for a one-time treatment, when in fact the eventual cost savings for a curative therapy accumulates over time.

To ensure that the nascent regenerative medicines sector advances so that patients in need will have access to these life-altering therapies, barriers to adoption of alternative payment models in both the public and private sectors -- specifically value-based purchasing agreements in which financing the costs of treatment, whether as annuitized payments or making future payments contingent on clinical outcomes or metrics -- must be addressed.

Medicaid Best Price and Average Manufacturing reporting requirements and Anti-Kickback Statute prohibitions are discussed below to provide examples of current regulations that have unintended consequences which are inhibiting the adoption of value-based, payment over time arrangements. They are highlighted to provide examples but are certainly not the only such legislative and regulatory barriers that need to be addressed.

***Medicaid Best Price and Average Manufacturing Reporting Requirements:*** Both Medicaid Best Price (BP) and Average Manufacturing Price (AMP) reporting requirements are main components that determine the rebate ultimately paid to the state Medicaid program and shared with CMS. ARM recognizes that they are both important tools to control the cost of therapies provided in the Medicaid program. However, they also pose significant hurdles that

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<sup>1</sup> Testimony of HHS Deputy Secretary Eric D. Hargan before the House Ways and Means Subcommittee on Health, July 17, 2018.

are forestalling the adoption of alternative payment models where the final reimbursement of therapy or service may occur when the treatment is administered. This poses limits to the development of and access to new potentially durable treatments.

For example, in a value-based purchasing arrangement there are questions as to how BP is to be determined if a payor finances the cost of a treatment through installment payments over a period of time and what are the rebate obligations. Additionally, in an agreement which sets reimbursement according to agreed upon levels of efficacy, it is unclear how a manufacturer that refunds all or a portion of the therapy cost for failure to meet those levels must then account for the refund as part of the calculation of BP.

The rebate formula's reliance on baseline AMP also poses particular concerns for value-based purchasing or other arrangements that utilize payment over time schedule. As an initial matter, it is unclear as to how such installment payments would be reported as the therapy's overall price for rebate calculation purposes. Should developers report only the purchase price paid at the time of the sale, *i.e.* the first installment, which would reflect only a portion of the drug's total purchase price? Would they need to report AMP in subsequent quarters cumulatively as what has been paid to date? Or would developers need to report the full payment upfront, even though this reported amount fails to correctly reflect the actual costs incurred by the Medicaid program during that first quarter and as such, distorts the rebate they must remit for a given period?

***Anti-Kickback Statute Prohibitions:*** Like the BP and AMP reporting requirements, Anti-Kickback Statute prohibitions (AKS) were adopted with a noble goal in mind – prohibiting transactions intended to induce or reward referrals for services or products reimbursed by federal health care programs. However, when the AKS was enacted over four decades ago policymakers could not have contemplated the scientific advances represented by regenerative medicines and the need to account for value-based payment models. As in the case of BP and AMP reporting requirements, AKS prohibitions are stifling the utilization of value-based contracting. For example, value-based arrangements may require certain ancillary services such as care coordination services or items that may be used for the collection and monitoring of clinical data. Such services could fall under the definition of the “remuneration” which, under current AKS regulation, is prohibited.

It is important to note that on August 27, 2018, the Department of Health and Human Services Office of Inspector General published a request for information (RFI), which said: “The Office of Inspector General (OIG) seeks to identify ways in which it might modify or add new safe harbors to the anti-kickback statute and exceptions to the beneficiary inducements’ civil monetary penalty (CMP) definition of ‘remuneration’ in order to foster arrangements that would promote care coordination and advance the delivery of value-based care, while also protecting against harms caused by fraud and abuse.” As of this writing, the OIG has not acted on this request as it relates to establishing safe harbors that address the AKS concerns of the regenerative medicine sector.

While both BP and AMP regulations provide for exceptions, they are narrowly focused and do not fully protect or address the value-based purchasing arrangements that are being contemplated for regenerative medicine therapies and developers are unsure of how to proceed.

- ARM Request: ARM urges Congress to support the necessary legislative and regulatory changes that will remove the current barriers to the adoption of value-based payment models.

### **Support Greater Access to New Technologies in the Inpatient Setting**

Many of these regenerative medicine treatments will be provided in the inpatient setting and are therefore covered and reimbursed under Medicare Part A. In 1983 when Congress created the Inpatient Prospective Payment System, regenerative and advanced technologies were closer to science fiction than the clinical reality they are today. At that time, Congress did not include a methodology that adequately reimburses hospitals for providing these types of new and innovative technologies.

However, in 2000, in order to recognize the value of new technologies, Congress required CMS to establish a mechanism to recognize the costs of new medical services and technologies in the inpatient setting for a minimum of two years and no more than three years. Furthermore, Congress instructed CMS that this additional payment could be satisfied by means of a new alternative known as an “add-on payment,” that is, a payment adjustment or any other similar mechanism for increasing the amount as long as it represented the estimated average cost of the service or technology. In response, CMS established criteria for a medical service or technology to receive a New Technology Add-On Payment (NTAP).

- ARM Request: ARM urges Congress to take several actions to improve the NTAP program to expedite access to new technologies: (1) Require CMS to increase the frequency of the current NTAP assignment process to no less than twice year. In doing so, hospitals can more easily afford to provide timely access to new and innovative therapies; (2) Extend the NTAP coverage period to four years from date of assignment of the NTAP to provide sufficient time for claims data to accumulate for the purposes of more accurately establishing a new relative weight or a new MS-DRG that accurately captures the cost of the new technology; and (3) Direct CMS to accept that the determination by the FDA that a therapy be considered under the RMAT or Breakthrough review pathway demonstrates that the substantial clinical improvement criteria has been met and CMS should not continue to use a different criteria standard.

### **Support Funding to Regulate Unregulated Stem Cell Clinics**

Mirroring the growth in the regenerative medicine sector, there has been, regrettably, a significant increase in the number of unregulated stem cell clinics marketing non-FDA approved products advertised directly to patients. It has been estimated that in 2009 there were two

stem clinics in the United States and by 2017 the number had grown to over 700<sup>2</sup>. A study published in early 2018 found that the number of new U.S. stem cell clinics with websites doubled on average every year between 2009 and 2014 and that up to 100 new websites appeared each year between 2014 and 2016<sup>3</sup>.

This explosion in the number of stem cell clinics has proven to be a significant oversight challenge for the FDA. In 2017, the agency announced that it would adopt a “risk-based” enforcement policy targeting the worst of the bad actors. Then-FDA Commissioner Scott Gottlieb stated at that time that “The rapid growth and promise of this field has increasingly sowed the ground for the entry of some unscrupulous actors, who have opportunistically seized on the clinical potential of regenerative medicine to make deceptive claims to patients about unproven and, in some cases, dangerous products. ... This underscores the importance of having a clear regulatory framework for developers and ensuring that those who skirt these regulations are held accountable.”

While ARM applauds the agency for this action and think it is a step in the right direction, we strongly believe that a “risk-based” enforcement approach is not robust enough to adequately regulate these burgeoning businesses. There must be strong, swift and consistent legal actions taken against questionable clinics in order to protect patients.

- **ARM Request:** ARM urges Congress to authorize increased funding for the FDA to effectively regulate the growing number stem cell clinics in the United States and take enforcement actions when necessary against bad actors to ensure the health and safety of patients.

### **Support Funding for Additional FDA Reviewers**

We are entering a critical time where it is predicted that regenerative medicines will be brought to market at a rapid pace in the next several years. ARM currently estimates that there are approximately 950 developers conducting over 1000 clinical trials worldwide, including 594 in Phase II and 95 in Phase III<sup>4</sup>. In January of this year, then-FDA Commissioner Scott Gottlieb and FDA’s Center for Biologics Evaluation and Research Director Dr. Peter Marks announced that, “We anticipate that by 2020 we will be receiving more than 200 INDs per year, building upon our total of more than 800 active cell-based or directly administered gene therapy INDs currently on file with the FDA. And by 2025, we predict that the FDA will be approving 10 to 20 cell and gene therapy products a year based on an assessment of the current pipeline and the clinical success rates of these products.”<sup>5</sup>

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<sup>2</sup> L. Turner, “The U.S. Direct-to-Consumer Marketplace for Autologous Stem Cell Interventions,” *Perspectives in Biology and Medicine* 61, no. 1 (2018): 7-24, <https://muse.jhu.edu/article/694817>

<sup>3</sup> P.S. Knoepfler and L.G. Turner, “The FDA and the U.S. Direct-to-Consumer Marketplace for Stem Cell Interventions: A Temporal Analysis,” *Regenerative Medicine* 13, no. 1 (2018): 19-27, <https://dx.doi.org/10.2217/rme-2017-0115>.

<sup>4</sup> Alliance for Regenerative Medicine, Q3 2019 Quarterly Report

<sup>5</sup> <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics>

In order to meet this challenge, the FDA needs a sufficient number of properly trained staff with the expertise to evaluate these applications. Included in the 21<sup>st</sup> Century Cures Act are provisions giving the agency with new hiring authorities designed to improve its ability to attract experienced personnel. However, additional financial resources were not provided. Additionally, recent government shutdowns have had an impact on the FDA's ability to attract qualified applicants and retain employees. Attracting and retaining this staff who can assess biologic license applications, particularly in a cutting-edge field that is evolving rapidly, is vital as the majority of these therapies are targeting rare or orphan diseases that often lack other clinically effective treatment options.

- ARM Request: Given the expected surge in the number of regenerative medicine applications in the next decade, it is crucial that the FDA attract and retain qualified personnel to evaluate these applications in an informed and timely manner. Therefore, the Committee should support an increase funding authorization levels for FDA reviewers.

#### **Expediting Access to New Technologies for Medicaid Patients**

Currently, many state Medicaid programs can take months before coverage for a newly FDA approved drug or biological is authorized. This is especially the case for regenerative medicines. During this time, many patients are denied access to these therapies that could literally change the course of their lives.

- ARM Request: Congress should require state Medicaid programs to cover all newly FDA approved drugs no later than ninety days from its approval date. This requirement mirrors the Medicare Part D's requirement of health plans for drugs in the six protected classes. In doing so, Congress will expedite access to newly approved technologies for society's most vulnerable and underserved patients.

In closing, ARM applauds you for your desire to continue to "modernize coverage and access to life-savings cures in the United States and across the globe." We appreciate your consideration of our recommendations and look forward to working with you on this very important initiative. Of course, please do not hesitate to contact me if you have any questions.

Sincerely,



Director, U.S. Policy and Advocacy