



July 16, 2018

The Honorable Alex Azar  
Secretary  
U.S. Department of Health and Human Services  
200 Independence Avenue S.W.  
Washington, D.C. 20201

Dear Secretary Azar:

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to comment on the Department of Health and Human Services (HHS) Request for Information (RFI), *HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs* published in the [Federal Register](#) on May 16, 2018.

ARM is a multi-stakeholder advocacy organization that promotes legislative, regulatory, and reimbursement initiatives necessary to facilitate access to life-giving advances in regenerative medicine globally. ARM comprises more than 275 leading life sciences companies, research institutions, investors, and patient groups 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 globally.

The regenerative medicine and advanced therapies sector is the next frontier in the fight against some of humankind's most devastating diseases and disorders. ARM estimates that as of year-end 2017, more than 850 regenerative medicine and advanced therapies developers are sponsoring 946 clinical trials across dozens of indications, including oncology, cardiovascular, central nervous system, musculoskeletal, bleeding and blood disorders, connective tissue disorders, metabolic disorders, ophthalmological disorders, and more.

We ask HHS to consider ARM's feedback to the RFI in the broader context of the diversity of technologies that comprise "regenerative medicines." While 'cell and gene therapies' are often included in the same category, there are important distinctions among these technologies that can have a bearing on how best to ensure patient access to them. In identifying these distinctions, ARM urges the Department to ensure that any future efforts to modernize the regulatory infrastructure for these therapies is sufficiently flexible to take into account the differences among technologies.

Cell therapy is the administration of viable, non-genetically modified cells into a patient's body to grow, replace or repair damaged tissue for the treatment of a disease. Cells can be administered allogeneically, in which the patient receives cells from a donor, or autologously, with patients receiving cells from his or her own body. ARM members are currently developing cell therapy approaches to treat a myriad of diseases and disorders, including but not limited to chronic heart failure, Crohn's disease, amyotrophic lateral sclerosis (ALS), ischemic stroke, diabetes, Parkinson's disease, and degenerative disk disease.

Tissue engineering combines scaffolds, cells and biologically active molecules into functional tissues to restore, maintain or improve damaged tissues. Biomaterials are medical devices designed to interact with living systems, providing physical structures and support for engineered tissues. ARM members are currently developing tissue-engineered products and biomaterials to treat cartilage damage and degeneration, wound repair, spinal cord injury, and hernia repair.

Gene therapy seeks to modify, replace, inactivate or introduce genes into a patient's body with the goal of durably treating, preventing or even curing disease. Gene therapy techniques include gene-modified cell therapy, which is genetic modification of a patient's cells outside of the body, followed by re-introduction of the modified cells to deliver a therapeutic effect. ARM members are developing gene therapies including but not limited to approaches to treat epidermolysis bullosa, inherited bleeding disorders (such as hemophilia A and B), inherited blood disorders (such as beta-thalassemia and sickle cell diseases), blood cancers (such as leukemia and lymphoma), inherited metabolic disorders (such as Hurler syndrome, Hunter syndrome, metachromatic leukodystrophy), inherited retinal disease, and Huntington's disease.

What is critical about all these technologies is that they can be transformative, potentially providing a durable therapeutic benefit with a single administration of the therapy. The potential for dramatic clinical benefit is why these innovations are changing medical care and transforming patient outcomes.

ARM encourages HHS to consider the potential value of these therapies to patients and society, and the need to enable new pricing and reimbursement approaches that can help make them available to patients. Given the diversity of regenerative medicine therapies, the conditions they address, and the contracting preferences of individual stakeholders, we expect that stakeholders may arrive at a variety of potential arrangements with different payers, including value-based arrangements (VBAs). However, existing regulations are not currently able to support the broad adoption of these alternative payment models, including certain VBAs. Thus, ARM's comments on the RFI, made in detail in the remainder of this letter, focus on the need to modernize the regulatory infrastructure and make recommendations to do so that take into account the promise of regenerative medicine therapies for patients and the healthcare system.

#### ***(A) Best Price Exemptions for Value-Based Arrangements***

HHS seeks feedback on how existing price reporting requirements (e.g., Best Price calculations under the Medicaid Drug Rebate Program) affect market incentives and the ability to implement certain VBAs.

##### ***ARM Recommendations:***

- ***Medicaid Best Price (BP) regulations should be updated to promote value based arrangements.***
- ***HHS should specify that a weighted price of the drug would be used for calculating the Best Price discount for Medicaid programs instead of using a single lowest price, which today discourages value-based arrangements.***
- ***Alternatively, CMS under its legal authority could exempt VBAs that meet certain criteria from the current Best Price reporting requirements, such that the prices and discounts that result from VBAs would be excluded from the calculation of Medicaid Best Price.***

- ***The HHS Office of Inspector General (OIG) should amend its Anti-Kickback Statute (AKS) safe harbor rules to better protect manufacturers that provide discounts based on patient outcomes.***

For Medicaid to cover prescription drugs, manufacturers must participate in the Medicaid Drug Rebate Program.<sup>1</sup> The Medicaid Drug Rebate Program requires manufacturers to provide rebates on drugs based on calculations that primarily use (a) the Best Price the manufacturer offers to any purchaser of the drug, and (b) the Average Manufacturer Price (AMP) paid by wholesalers and retail pharmacies for the drug.<sup>2</sup> However, such requirements do not account for payment mechanisms that link a therapy's final price with the clinical outcomes that patients achieve. Thus, the law could hamper manufacturers and payers that wish to experiment with VBAs.

For example, if the terms of a commercial VBA contract require a manufacturer to provide a full rebate for the cost of a regenerative medicine therapy when the desired clinical outcome is not achieved, Medicaid "best price" would be affected if that contractual condition is triggered. For that same regenerative medicine therapy administered to a Medicaid beneficiary, under current regulations, state Medicaid programs would receive the drug for free after rebates for all future patients because its Best Price would be \$0, regardless of an individual patient's clinical outcome. That would discourage innovative payment models that drive value for patients. Moreover, because of the statutory link between the Medicaid Drug Rebate Program and the 340B Drug Pricing Program,<sup>3</sup> the manufacturer may be required to offer that same regenerative medicine therapy under this scenario to 340B covered entities at \$0.01 for purchase.<sup>4</sup> Again, such an impact is without regard to the clinical outcome of the patient being treated and would be untenable.

Depending on the payer and site of service mixes, current Best Price law would have the effect of discouraging innovative payment models that drive value for patients and limit risks for payers. Notably, the Congressional Budget Office (CBO) has previously stated that the Best Price law's inflexibility "may have had unintended consequences for both Medicaid and non-Medicaid purchasers."

ARM encourages clarification and pathways to enable Medicaid Best Price regulations to allow more VBA contracts between payers and manufacturers. For example, CMS possesses the legal authority to exempt VBA contracts that meet certain criteria from the current best price reporting requirements, such that the prices and discounts that result from VBA contracts be excluded from calculation of Medicaid Best Price.

Alternatively, under its authority, HHS could specify that a weighted price of the drug would be used for calculating the Best Price discount for Medicaid programs instead of using a single lowest price, which today discourages VBA arrangements. For example, a manufacturer that offers a 100% rebate as part of a guarantee for a group of patients where the drug fails to meet a quality standard for only 10% of the patients would be giving an average rebate of only 10%. Under this new calculation, the guarantee

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<sup>1</sup> See Social Security Act ("SSA") § 1927(a)(1), 42 U.S.C.S. § 1396r-8(a)(1) (LexisNexis 2018) (requiring Medicaid payment for a "covered outpatient drug" if its manufacturer has "entered into" and has "in effect" a Medicaid Drug Rebate Agreement).

<sup>2</sup> See SSA § 1927(c), 42 U.S.C.S. § 1396r-8(c) (LexisNexis 2018).

<sup>3</sup> See 42 U.S.C.S. § 256b(a)(1) (LexisNexis 2018).

<sup>4</sup> See 42 C.F.R. § 10.10(b) (Lexis Nexis 2018) (describing the penny pricing policy when the 340B ceiling price would otherwise be \$0).

would not trigger the Best Price rule because the 10% rebate level would be less than any of Medicaid's mandated discounts.

It is important to note that in order to facilitate VBA contracts, the HHS Office of Inspector General (OIG) would also need to amend its AKS safe harbor rules<sup>5</sup> to better protect manufacturers that provide discounts based on outcomes. Otherwise, under existing law, OIG could perceive these arrangements as inducements.<sup>6</sup> OIG should use its existing authority to include VBA contracts as an AKS safe harbor. Absent these collective regulatory changes, new payment models that drive innovation will be stymied.

### ***(B) VBAs and Price Reporting***

#### ***ARM Recommendations:***

- ***HHS should recognize the important role of VBAs and the unique value of regenerative medicine and their potential for transformative and durable improvements in patient health outcomes, and the importance of maximizing the ability of patients to access that value.***
- ***A one-size fits all reimbursement model is not feasible. Regulatory flexibility to account for many disease areas and patient population(s) is essential.***
- ***Many payment models should be advanced to enable patient access while addressing payer ability to cover upfront costs and support innovation. ARM encourages CMS to test VBAs in Medicare/Medicaid that support regenerative medicine therapies and address the regulatory barriers impeding innovation. Further, we encourage HHS to make this a budget priority and that deployment of such models be expedited.***
- ***We urge HHS to host a stakeholder meeting to discuss new potential VBA approaches.***
- ***We recommend that HHS work with the National Quality Forum and patient, provider, and industry stakeholders to develop meaningful quality metrics that reflect the value of regenerative medicine.***

HHS seeks feedback on potential benefits or unintended harms from excluding manufacturers involved in VBA contracts from statutory price reporting programs for drugs subject to such contracts. HHS also requests comment on potential modifications to regulatory definitions to encourage VBA contract uptake among manufacturers.

ARM appreciates the Administration's desire to develop value-based approaches to pay for drugs. As noted above, regenerative medicine therapies provide a great deal of value to patients and also provide cost savings that are important to the healthcare system. In many cases, the cost to society of not having a treatment (that is, the direct and indirect costs of the disease) is already a burden to patients, their caregivers, and the healthcare system. The overall cost of illness encompasses many aspects of the disease that impact on our nation's health outcomes. These aspects range from the incidence or prevalence of disease to its effect on longevity, decrease in health status and quality of life, and productivity.

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<sup>5</sup> See 42 C.F.R. § 1001.952 (LexisNexis 2018).

<sup>6</sup> See 42 U.S.C. § 1320a-7b(b)(2) (LexisNexis 2018).

Regenerative medicine therapies have the potential to add value to patients' lives and offset significant direct and indirect costs to our nation's healthcare system. These therapies can eliminate in some cases long-term therapy and further avert downstream costs associated with complications of disease progression and hospitalization. However, to achieve these savings, innovative payment and financing models must be developed to support patient access to transformational regenerative medicine treatments, some of which may require only a single administration.

Enabling pricing and reimbursement approaches that allow payers, providers and manufacturers to arrive at VBAs is essential to ensure patients have access to these life-saving therapies. The FDA's new regenerative medicine advanced therapy (RMAT) designation means that more therapies are moving quickly through the approval process and into the market. As a result, payers, including Medicare and Medicaid, should expect to see several new regenerative medicines available every year. Accordingly, ARM encourages HHS to quickly advance models that allow these regenerative medicine therapies to provide value to patients.

It is also important that multiple new payment and financing models are advanced to reflect unique disease and product characteristics. Product characteristics, payer needs, current reimbursement mechanisms and innovator needs may vary case-by-case. There is no "one size fits all" approach. The variety of technologies and approaches means that multiple options are needed, and in some cases will need to be combined. For example, pay-for-performance arrangements could be combined with a one-time payment or alternatively with payments over time/installment payments.

The key benefits with these payment models are that payers and manufacturers would be able to negotiate ways to address uncertainty of product performance, as well as to moderate the short-term financial risk of a large upfront price with the expectation of continued benefits.

These contracts have the potential to align the interests of patients, health plans, and manufacturers around the shared goal of ensuring efficient use of health care resources while preserving access to care and incentives for innovation. We are already seeing manufacturers and payers align on targeted innovative outcomes-based contracts. For example, Spark Therapeutics proposed an outcomes-based model for voretigene neparvovec-rzyl (LUXTURNA™) at launch. LUXTURNA is the first FDA-approved adeno-associated virus (AAV) vector-based gene therapy indicated in the United States for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy (a recessive blinding disease). Spark Therapeutics has agreed to share risk with commercial insurers by paying rebates if the patient outcomes fail to meet a specified threshold using a full-field light sensitivity threshold (FST) test, thereby linking the payment for LUXTURNA to both short-term efficacy (30-90 days) and longer-term durability (30 months) measures that are unique to this one-time gene therapy. Spark also has submitted a proposal to CMS to conduct a demonstration project for LUXTURNA that would enable Spark to offer both commercial and government payers an installment payment option, as well as greater rebates tied to clinical outcomes.

ARM encourages CMS to work with manufacturers to advance such models to help inform future VBA proposals, while simultaneously evaluating opportunities to modify existing regulations that impede innovation. Specifically, ARM encourages CMS to use the full extent of its existing authority to experiment with novel payment models, that HHS make this a budget priority, that the review and deployment of such demonstrations be expedited, and that a meeting be convened of stakeholders for an open dialogue on potential new payment approaches and specific guidance needed to enable them.

It is important to note that each VBA model may have different associated barriers that need to be addressed by HHS. A specific problem for Medicaid VBA contracts is the difficulty of structuring such contracts in excess of one year due to state budget cycles typically being for a single year. Multi-year VBAs also raise the issue of “patient switching” across payer types (though payers have anecdotally expressed various levels of concern with this issue). Specifically, a situation could arise in which a payer may negotiate a multi-year VBA with a manufacturer, the patient receives the therapy, but then the patient “switches” to another insurance plan before the VBA contract term has concluded. HHS should work with stakeholders to consider how to address the uncertainty that patient switching can create.

Another barrier is that traditional payment and financing models do not capture quality metrics that are appropriate for curative regenerative medicine therapies. VBA contracts will likely require flexibility to include quality measurement that meaningfully captures the value of regenerative medicine therapies under appropriate time parameters over multiple years. This could include a quality metric that captures a demonstrated clinical trial endpoint that has not routinely been tracked under the Medicare/Medicaid program or a metric that distinguishes the value of a one-time, curative treatment versus one that realizes similar total health gains but over a number of years. Supporting the development of such metrics would help ensure patient access to innovative treatments and vital services that have the potential to help patients with complex diseases that have never before been effectively treated. We encourage HHS to work with the National Quality Forum (NQF) and patient, provider and industry stakeholders to develop meaningful quality metrics that reflect the value of regenerative medicine therapies.

Other impediments to VBA arrangements stem from laws and regulations that inadvertently create obstacles to VBA contracts such as the AKS, as noted above. Many existing laws and regulations were written with traditional fee-for-service (FFS) transactions in mind, and not for the VBA contracts that manufacturers and payers are exploring today for regenerative medicine therapies. Accordingly, we strongly encourage OIG to include appropriate forms of VBA contracts for regenerative medicine therapies in the AKS safe harbor regulations. As discussed above, we urge CMS to consider a regulatory exception for certain price concessions associated with VBAs and specific regulations to provide better instruction and consistency when reporting VBAs as well as potential payment over time structures. Such exceptions would mitigate the effect of outcome-based arrangements on Average Sales Price (ASP) and resulting potential risk to appropriate provider reimbursement, as well as the potential significant impact of such pricing arrangements on a therapy’s Best Price, Average Manufacturer Price (AMP), ASP and first quarter base AMP, if outcomes-based VBAs are not treated distinctively.

Given the considerations noted above, ensuring that the regulatory system is sufficiently flexible to accommodate value-based payment solutions will require significant innovation and collaboration among all stakeholders, including the Department, State Medicaid Agencies, commercial payers, patients, providers, and industry.. As such, ARM looks forward to working with HHS to develop delivery and payment models that support the innovative regenerative medicine therapies on the horizon.

### ***(C) Long-Term Financing Models***

#### ***ARM Recommendations:***

- ***HHS should explore long term-financing approaches, including but not limited to, payment over time, with payments spread out over a defined number of years.***

- **HHS should decrease barriers to long-term financing models solutions that are posed by Medicaid Best Price requirements. CMS also should extend the AMP and Best Price restatement period beyond the current 3-year timeframe VBAs.**

HHS requests feedback on long-term financing models to enable payments for high-cost treatments to span multiple years. Key issues include assumption of financial risk, how Medicare and Medicaid could account for future costs saved from regenerative medicine therapies, and regulations CMS could consider revising to allow more flexibility in these arrangements for both public and private payers.

The rapid pace of innovation means that the need for long-term financing for regenerative medicine therapies could quickly become critical for the healthcare system. As noted by FDA Commissioner Scott Gottlieb, “We are at a key point when it comes to cell and gene therapy. These therapies have the potential to address hundreds, if not thousands, of different rare and common diseases. For a long time, they were largely theoretical constructs. Now they’re a therapeutic reality.”<sup>7</sup> To advance the progress noted by Commissioner Gottlieb, we must create meaningful long-term financing models to support regenerative medicine therapies.

Now that transformative regenerative medicine therapies products have been approved, stakeholders should work together to maximize patient access to medicines that can transform lives while encouraging continued scientific innovation in regenerative medicine. One long-term financing approach that may foster patient access involves payment over time, which would be multiple installment payments to manufacturers over a set time period (e.g. annual payments for a five-year period). The benefits of the installment model “includes the potential to reward innovation and to better align costs with the time period over which benefits are delivered to the patient, thereby reducing up-front budget impact to the payer or provider and reducing initial cost as a barrier to appropriate access for treatment-eligible patients.”<sup>8</sup>

Such a long-term financing model could also be supported in alternative payment models like Accountable Care Organizations (ACOs) that share risk across stakeholders. To date, neither traditional FFS payments nor alternative payment models account for one-time administered, potentially curative innovations. Rather than viewing payment reforms for regenerative medicine therapies and for health care providers as distinct, CMS could encourage developers of alternative payment models, through the Physician Technical Advisory Committee (PTAC) and CMMI to engage on ways to maximize the value brought by new technologies. For example, this could include model frameworks and regulatory clarifications for sharing data related to the benefits and risks of new technologies for particular patients, or for incorporating drug and device shared accountability in ACOs and bundled payments.

These models are, however, not without some challenges, at least under existing price reporting requirements. Specifically, as discussed previously, the extended timeline for payment triggers AMP and Medicaid Best Price reporting challenges. This includes the need to clarify appropriate treatment of the time-value of money to avoid undue burden from adjustments based on timing of cash flows for

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<sup>7</sup> Scott Gottlieb, MD, Commissioner, FDA, Keynote Address at the Alliance for Regenerative Medicine Annual Dinner & Legislative Fly-In (May 22, 2018).

<sup>8</sup> Ted Slocumb and Michael Werner, *New Payment And Financing Models For Curative Regenerative Medicines*, IN VIVO PHARMA INTELLIGENCE (July 24, 2017), <https://invivo.pharmaintelligence.informa.com/IV005132/New-Payment-And-Financing-Models-For-Curative-Regenerative-Medicines>.

payment over time. CMS also may need to confirm the three-year AMP and Best Price restatement period for value-based contracts extending beyond three years. As noted in a recent article authored by ARM in *In Vivo*, “there are potential solutions which include dividing the initial costs of the treatment into smaller payments payable over time, perhaps without tying the payment to performance, survival or continued coverage by the patient’s original plan.” Ongoing payments could be made part of the patient’s pre-existing condition or covered under essential health benefits to ensure continuity of coverage. If many payers engage in these types of arrangements, the flow of patients, costs and benefits across plans should eventually balance out.”<sup>9</sup>

***(D) Site neutrality for Physician-Administered Drugs***

***ARM Recommendations:***

- ***The site of care for regenerative medicine therapies vary, and decisions on settings of care should be left to providers, in conjunction for their patients, based on individual clinical circumstances alone, and not financial incentives put in place by regulations.***
- ***HHS should consider testing a site neutrality payment pilot under CMMI. CMMI should use its authority to waive inpatient MS-DRG payment requirements to test site neutrality payment for providers currently administering regenerative medicine therapies.***

HHS requests feedback on potential impacts of site-neutral payment policies, including effects on healthcare system organizations, the competition for specific healthcare services, and how the differences between Medicare Part A coverage and Part B coverage may impact affordability and access for beneficiaries. Further, HHS requests feedback on specific CMS policies that currently create barriers to site-neutral payments, and how patient safety could be impacted by encouraging the shift of some services to outpatient settings.

The variation in how regenerative medicines therapies are reimbursed under different sites of care has the potential to create significant disparity in provider incentives to treat patients in one site of care over another. Due to the different payment structures between settings (e.g., in the inpatient setting, drugs are paid under a bundled Medicare Severity-Diagnosis Related Groups (MS-DRGs) whereas in the outpatient setting, separately paid therapies are paid at ASP + 6 %), there may be disincentives for providers to treat in an inpatient setting, even if that is in the best interest of the patient based on clinical and safety factors.

The ultimate goal of creating site neutrality for physician-administered treatments is to eliminate the incentive structure to choose a site of care based on anything other than what makes the most sense for patients. Guaranteeing site neutrality across settings of care could also facilitate patient access by reducing payment uncertainty for providers operating under the MS-DRG payment system. HHS may consider testing a site neutrality payment pilot for Medicare providers via CMMI under their authority. CMMI may use that authority to waive inpatient MS-DRG payment requirements to test site neutrality payment for rare diseases, including those treated with regenerative medicine therapies, where the MS-DRG payment does not capture the total cost of care, including the cost of administering the treatment.

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<sup>9</sup> Ted Slocomb, Michael Werner, Ted Haack, Satish Valluri and Beth Rader, *New Payment And Financing Models For Curative Regenerative Medicines*, In Vivo Pharma Intelligence (July/August 2017), [https://www.hklaw.com/files/Uploads/Documents/Articles/ARM\\_Curative\\_Regenerative\\_IV1707\\_LRS.pdf](https://www.hklaw.com/files/Uploads/Documents/Articles/ARM_Curative_Regenerative_IV1707_LRS.pdf)



## **Conclusion**

ARM appreciates this opportunity to submit comments regarding the Administration's RFI to lower prescription drug costs and patient spending. We appreciate your consideration of our viewpoints on this important issue and look forward to working with the Administration to address the issues outlined in this RFI response and to ensure that the value of regenerative medicine therapies is recognized in payment and financing models. Should you have any questions regarding this response, please contact Robert Falb at [rfalb@alliancerm.org](mailto:rfalb@alliancerm.org) or Miranda Franco at [miranda.franco@hklaw.com](mailto:miranda.franco@hklaw.com).