June 6, 2023

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Ave, SW
Washington, DC 20201

Submitted via http://www.regulations.gov

Medicare Program; Proposed Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Policy Changes and Fiscal Year 2024 Rates; Quality Programs and Medicare Promoting Interoperability Program Requirements for Eligible Hospitals and Critical Access Hospitals; Rural Emergency Hospital and Physician- Owned Hospital Requirements; and Provider and Supplier Disclosure of Ownership (CMS-1785-P)

Dear Administrator Brooks-LaSure:

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS) proposed payment updates to the fiscal year 2024 Hospital Inpatient Prospective Payment System (Proposed Rule).[1]

ARM is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. As a community, ARM builds the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and advancing the narrative with data and analysis. We actively engage key stakeholders to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from durable, potentially curative treatments. As the global voice of the sector, we represent more than 475 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations. As of year-end 2022, there were 1,457 engineered cell therapy and genetic medicine developers worldwide sponsoring 1,070 clinical trials (out of 2,200 clinical trials globally, which are also sponsored by academic and government institutions) across dozens of indications, including rare monogenetic diseases, oncology,

[1] 88 Fed. Reg. 26,658 (May 1, 2023).

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cardiovascular, central nervous system, musculoskeletal, metabolic disorders, ophthalmological disorders, and more.[2]

As described in greater detail below, ARM urges CMS to adopt its coding proposals for MS-DRG 018 but to continue to use the proxy of standardized drug charges of less than $373,000 to identify clinical trial claims and expanded access use cases when calculating the average cost for MS-DRG 018. Additionally, ARM urges CMS to implement a biannual NTAP application and start date process to reduce Agency workload instead of its current proposals. Finally, ARM is disappointed that CMS did not follow up on its Request for Information (RFI) on potential new reimbursement methodologies for low-volume high-cost drugs post NTAP from the FY 2023 rulemaking process.

Comments Related to The Relative Weight of MS-DRG 018

I. CMS Should Ensure Any Policies Adopted in the Final Rule Maintain a Stable Relative Weight for MS-DRG 018.

ARM thanks CMS for its efforts towards creating and now maintaining a stable relative weight for MS-DRG 018. CMS proposes two changes to the methodology for identifying clinical trial claims and expanded access use claims in MS-DRG 018. Specifically, CMS proposes to:

(1) exclude claims with the presence of condition code "90" (or, for FY 2024 rate setting, the presence of condition code "ZB") and claims that contain ICD-10-CM diagnosis code Z00.6 without payer only code "ZC" that group to MS–DRG 018 when calculating the average cost for MS–DRG 018; and,

(2) no longer use the proxy of standardized drug charges of less than $373,000 to identify clinical trial claims and expanded access use cases when calculating the average cost for MS–DRG 018.

ARM supports this first proposal to exclude the specified claims when calculating the average cost for MS-DRG 018 because it reinforces current billing practices, is consistent with CMS' coding principles and will likely provide greater accuracy with claim identification for rate setting purposes. This in turn should lead to a more predictable and stable relative weight.

However, ARM urges CMS not to finalize its proposal to simultaneously eliminate its use of the proxy of standardized drug charges of less than $373,000 to identify claims to be excluded from rate setting. Historically poor hospital coding practices caused CMS to use this proxy for its claim identification. ARM appreciates CMS' statement that "we believe that providers have continued to gain experience with the use of ICD–10–CM diagnosis code Z00.6 to report cases involving a clinical trial of a cell therapy. This is supported by our

[2] https://www.alliancerm.org

observation that the percentage of claims reporting standardized drug charges of less than $373,000 that do not report ICD–10–CM code Z00.6 relative to all claims that group to MS–DRG 018 fell significantly from the FY 2019 data (used in the FY 2021 rate setting) to the FY 2022 data (used in the FY 2024 rate setting)."[3]

While this data is encouraging, ARM is still concerned that hospitals may still not accurately or appropriately code clinical trial or expanded access cases. There were 65 cases in the 2021 MedPAR data mapped to DRG 018 with standardized drug charges less than $373K. In FY 2023, there were 398 cases used in rate setting for MS-DRG 018, which could increase the case volume by 16% if CMS makes this change. Therefore, CMS should still use the proxy of standardized drug charges of less than $373,000 to identify and exclude these cases when calculating the average cost for MS–DRG 018 for at least one more year. In doing so, CMS will have another year of data to rely on that will hopefully reflect hospitals are properly coding all CAR-T cases. ARM believes that this will likely ensure a stable and predictable relative rate for MS-DRG 018 for FY 2025.

II. CMS Must Carefully Balance Adding New Therapies to MS-DRG 018 With Maintaining Stable Relative Weights and Beneficiary Access

ARM continues to advocate that CMS be flexible in establishing reimbursement policies that result in accurate payment, promote innovation, and ensure timely access for Medicare beneficiaries to these innovations. ARM believes that the current construct of MS-DRG 018 protects the stability of the relative weight, and appreciates the Agency's historic statements that it will continue to evaluate "the creation and assignment of multiple MS–DRGs for cell and gene therapy cases: One to cover patient care costs, the other to cover product costs across therapeutic product categories."[4] However, as more therapies come to market **ARM urges CMS to further detail the circumstances under which it will create new MS-DRGs for cell and gene therapies.** ARM believes that this information will provide transparency and predictability to manufacturers supporting their commercialization efforts in the inpatient site of care. In doing so, CMS will hopefully maintain the goal of ensuring a stable and accurate provider reimbursement and therefore, patient access to all novel therapies.

Comments Related to New Technology Add-on Payment (NTAP) Process

Congress enacted the NTAP program to facilitate access to new therapies and technologies. The NTAP statute requires that a new technology represent an advance in medical technology that substantially improves the diagnosis or treatment of individuals to be eligible for NTAP.[5] Regenerative medicine, cell and gene, and advanced therapies epitomize such advances. In fact, the Accelerated Approval, Priority Review, Fast Track, and the regenerative medicine advanced therapy (RMAT) designations require the manufacturer to demonstrate many of the

[3] 88 Fed. Reg. at 26,774.
[4] 87 Fed. Reg. 28,108, 28,131 (May 10, 2022).
[5] *See* SSA §1886(d)(5)(K)(vii).

characteristics required to obtain NTAP. To mitigate barriers to uptake for these innovative therapies, ARM urges CMS to reverse course with its proposed timing changes to the NTAP application process and instead implement a biannual process for making NTAP determinations. Additionally, ARM urges CMS to adopt certain additional improvements to the NTAP program as stated below.

I. Requiring an FDA Acceptance or Filling Letter Within a Biannual Process Appropriately Balances the Goals of Reducing Agency Workload with Promoting Beneficiary Access.

CMS proposes two modifications to the NTAP process. First, CMS proposes to require future applicants to have a complete and active FDA market authorization request at the time of the NTAP application submission. Second, CMS proposes to move the FDA marketing authorization deadline from July 1 to May 1. If finalized, these new requirements would begin with NTAP applications for FY 2025. Taken together, these process changes may reduce Agency workload as CMS intends but would do so at the likely expense of beneficiary access to innovative cell and gene therapies. Rather, ARM recommends that CMS adopt a biannual NTAP application process to promote access to innovative therapies while also addressing the agency's workload concerns. Unless and until CMS adopts such a process, CMS should not finalize its proposal to require submission of an FDA acceptance or filing letter as a condition for submitting an NTAP application.

A. Current NTAP Proposals Ignore FDA's Timelines and will Therefore Elongate the Time to Access.

As noted above, CMS is proposing to require future applicants to have a complete and active FDA market authorization request at the time of the NTAP application submission. CMS clarifies that submission of a request for marketing authorization to the FDA means that the applicant has submitted a complete application to the FDA, has received an FDA acceptance or filing letter, and that the application has an active status with FDA. CMS states that combining this requirement with the earlier May 1 deadline would "further increase transparency and improve the evaluation process" while also allowing "adequate time to fully evaluate the new technology." CMS believes that these new criteria strike the appropriate balance between providing adequate time to fully evaluate the applications while also continuing to preserve flexibility for manufacturers. ARM respectfully disagrees.

Instead, these proposals ignore important FDA regulatory timelines and, if finalized, would arbitrarily delay access to innovative therapies based solely on when FDA makes certain regulatory determinations for a given product. For example, a decision about granting priority review is made by the FDA within 60 calendar days of the FDA's receipt of the marketing application or efficacy supplement. If priority review is granted, CBER has a 6-month goal for reviewing the biologics license application (BLA) or efficacy supplement.[6] This means that the

[6] https://www.fda.gov/media/120267/download

time from BLA submission to CBER approval can be as brief as 8 months. Depending on when the BLA is submitted, under CMS's proposal, a cell or gene therapy undergoing priority review can be FDA approved for well over a year prior to NTAP being available.

Specifically, assume a cell and gene therapy manufacturer submits its BLA to the FDA on November 1. The FDA grants priority review within 60 days (i.e., by January 1) and then grants approval within 6 months—well ahead of CMS' current July 1 deadline and, depending on FDA's timing, potentially prior to CMS' proposed May 1 deadline. However, applying CMS' proposed requirement for an FDA acceptance or filing letter, the manufacturer would not have applied for an NTAP for its first fiscal year post-approval because the manufacturer would not have had such a letter by the October NTAP submission deadline. Thus, instead of the NTAP initiating the October immediately following FDA approval, hospitals would be required to wait an additional fiscal year—at least 16 months post-approval—for the product's NTAP to take effect. Below is an example of the potential impact of these policies on a hypothetical technology approved and marketed on June 30, 2025.

Current Policy			**Proposed Policy**		
NTAP Application Deadline	**NTAP Effective Date**	**NTAP End Date**	**NTAP Application Deadline**	**NTAP Effective Date**	**NTAP End Date**
October 2024	October 1, 2025	September 30, 2028	October 2025	October 1, 2026	September 30, 2028

ARM is very concerned about the potential impact of this policy on Medicare beneficiaries. As outlined in Appendix A, all the recent FDA approved cell and gene therapies received a priority review such that some of these therapies could wind up in a situation where the therapy is FDA approved and the NTAP starts 17 months later. In light of these consequences, **ARM can support CMS's proposal to require an FDA acceptance or filling letter only if the NTAP application process is transitioned to be biannual**, as described in the subsequent section of this letter.

B. CMS Should Implement a Biannual NTAP Application Process.

As described in the Proposed Rule, under the current annual NTAP determination process, "[t]he volume of new technology add-on payment applications has risen substantially," rising by 200 percent between FY 2020 to FY 2024, while simultaneously increasing in complexity, making it more challenging for CMS to review its policies during the rulemaking cycle.[7] The annual NTAP determination process also has downsides for patients: providing a single opportunity to obtain NTAP for a given fiscal year can result in significant delays before a product can obtain NTAP post-approval, which can hinder uptake of innovative new therapies to the detriment of Medicare beneficiaries.

[7] Id. at 26,962.

ARM appreciates the burden on CMS of reviewing a rising number of increasingly complex NTAP applications in the short span of a single rulemaking cycle. However, any solution to address this workload issue must also consider the potential impact to beneficiaries. ARM believes a better solution would be to implement a biannual NTAP application process. Specifically, CMS should establish two annual NTAP determinations, with effective dates of October 1 and April 1 of each fiscal year.

Consistent with the statute, any NTAP application process must include a stakeholder meeting and the solicitation of public comment. ARM also shares CMS' goal of "ensuring that the public has sufficient information to facilitate public comment on whether the medical service or technology meets the new technology add-on payment criteria."[8] Further, ARM agrees with CMS that one of the goals of the NTAP is to provide "the public and the agency would be able to more knowledgeably analyze the new technology add-on payment applications and supporting data and evidence to inform an assessment of the technology's eligibility for the add-on payment."[9] These are foundational concepts that should always be part of the NTAP process and not compromised by CMS.

A biannual NTAP application process that builds in time for the requisite stakeholder meeting and informed public input could be structured as follows:

For the October 1 NTAP start date:

* NTAP application due April 1.
* Public meeting in early/mid-May.[10]
* NTAP proposals issued in early/mid-June.
* 30-day comment period.
* CMS publishes final NTAP decisions in late August/no later than September 1.
* October 1 effective date.

For the April 1 NTAP start date:

* NTAP application due October 1.
* Public meeting in early/mid-November.[11]
* NTAP proposals issued in early/mid-December.
* 30-day comment period.
* CMS publishes final NTAP decisions at end of Feb./no later than March 1.
* April 1 effective date.

ARM believes these proposed timelines for a biannual NTAP application process would satisfy CMS' stated goals and the statutory requirement to provide

[8] Id. at 26,961.
[9] Id.
[10] Id.
[11] SSA §1886(d)(5)(K)(vii)(III).

for a stakeholder meeting on NTAP applications.[12] Further, more NTAP determinations would enhance the quality of data for the Agency to use for rate setting purposes. In adding a second effective date for NTAPs each year CMS would, in theory, have more claims data associated with the new technology to analyze when establishing the next fiscal year's relative weights and provide access to new technologies quicker to Medicare beneficiaries.

The timelines outlined above would also give the public a 30-day comment period to provide comments on the each proposed NTAP application. We recognize the agency's obligation to establish any requirement that "establishes or changes a substantive legal standard . . . governing the payment for services" through rulemaking with a 60-day comment period.[13] However, we believe CMS could satisfy this requirement by going through notice-and-comment rulemaking to establish the substantive legal standards used to determine whether a product qualifies for NTAP, as well as the process—including the opportunity for public comment—for applying those standards. Once those standards were established, CMS would apply them outside of rulemaking on a biannual basis. We note there is ample precedent for similar approaches under the Medicare program, including the Clinical Laboratory Fee Schedule rate setting process,[14] and the process for approving pass-through payment applications under the Hospital Outpatient Prospective Payment System.[15]

The biannual NTAP application is thus a legally sufficient solution that strikes the appropriate balance of managing CMS' workload while expediting access to cell and gene therapies.

II. ARM Urges CMS to Evolve its NTAP Eligibility Polices to Further Promote Access to Innovative Therapies

A. Similar to Devices, CMS Should Recognize Certain FDA Approval Designations For Drugs As Dispositive for Newness and Substantial Clinical Improvement NTAP Criteria.

For FY 2020, CMS implemented a dramatic change in the eligibility criteria for certain devices but not for drugs or biologicals that meet a very similar evidentiary standard. Specifically, starting in FY 2020, if a medical device is part of the FDA's Breakthrough Devices Program and received FDA marketing authorization, it would be considered new and not substantially similar to an existing technology for purposes of the new technology add-on payment under the IPPS.[16] Additionally, CMS states that because the technology may not have a sufficient evidence base to demonstrate substantial clinical improvement at the time of FDA marketing authorization, the medical device would not need to meet the substantial clinical

[12] Id.
[13] SSA § 1871(a)(2).
[14] 42 CFR part 414, subpart G.
[15] 42 CFR part 419, subpart G.
[16] 87 Fed. Reg. at 28,026.

improvement requirement.[17] CMS states that it received 17 applications for new technology add-on payments for FY 2023 under this alternative NTAP pathway.[18] ARM views this as a successful policy change and urges CMS to add drugs and biologicals to this recent policy change. Such an approach would signal support for more and better patient access to transformative medical devices and drugs.

For FY 2020, CMS denied adding drugs to this policy stating that the "current drug-pricing system provides generous incentives for innovation, but too often fails to deliver important medications at an affordable cost. Making this policy applicable to drugs would further incentive innovation but without decreasing cost, a key priority of this Administration." ARM respectfully disagrees, especially considering the increase in device applications, and urges CMS to revisit this conclusion to be consistent in its approach to promoting access to all innovative technologies and include drugs and biologicals within the same alternative pathway as applied to devices. Finally, by treating Breakthrough devices and drugs equally, CMS will reduce its workload because it will only have to analyze the cost criterion for the NTAP applications for all products with Breakthrough status.

B. CMS Should Increase the NTAP Payment Cap to Eighty Percent

ARM appreciates CMS' recently implemented NTAP payment rate which equals the lessor of the costs of the new medical service or technology; or 65 percent of the amount by which the costs of the case exceed the standard DRG payment. The overall NTAP reimbursement formula, however, deflates the overall amount because it focuses on an amount that is the "lesser of" two calculations. Congress instructed CMS to reimburse hospitals an amount that reflects the estimated average cost of the technology. ARM respectfully disagrees that the 65 percent payment rate within the current "lessor of" formula satisfies Congressional intent. ARM remains concerned that while the 65 percent is an improvement over 50 percent, this payment amount still does not adequately reimburse hospitals for providing a new technology.

ARM, therefore, urges CMS to cap this rate at 80 percent, consistent with the outlier percentage. Based on ARM's historical data analyses, 65 percent would still require many hospitals to significantly mark-up the cost of the new technology in order to break even, whereas, with an 80 percent cap those hospitals with more conservative mark-up practices can still provide access to beneficiaries. This is clearly demonstrated with current charging practices of hospitals of CAR T-cell therapies. As a general principle, ARM believes that CMS' NTAP payment methodology must be practicable from an implementation point of view at the hospital level while simultaneously allowing for equal beneficiary access in the inpatient setting. The American Hospital Association also asserts that a longer-term approach is needed to ensure access to these therapies.[19]

[17] 84 Fed. Reg. at 19,372.
[18] 88 Fed. Reg. at 26,924.
[19] https://www.aha.org

Comments Related to CMS FY 2023 Request for Information on Access to Orphan Drugs

As stated above, ARM supports CMS' efforts to create accurate and transparent payment rates for innovative therapies such as cell and gene therapies. Many of these technologies will have orphan designation and, as we have stated previously, there are several barriers that providers face in treating beneficiaries with these orphan designated drugs in the Medicare hospital inpatient setting. CMS stated in its FY 2019 rulemaking that "it is not appropriate for facilities to deny treatment to beneficiaries needing a specific type of therapy or treatment that involves increased costs."[20] ARM believes this could still be the case and was hopeful that CMS would propose solutions to these access barriers based on last year's request for information (RFI). ARM is disappointed that CMS provided no proposals in response to stakeholder feedback, and we resubmit our previous suggestions on how to break down some access barriers to low volume high-cost drugs post NTAP, especially cell and gene therapies.

First, ARM urges CMS to require hospitals to report to CMS the timelines of when the orphan drug was either added to the hospital formulary and/or timely and appropriately dispensed. In doing so, ARM believes that CMS can both stimulate and equalize amongst all hospitals timely access to new therapies for Medicare beneficiaries while holding hospitals accountable for unnecessary access delays.

Second, ARM completely agrees with CMS that when "Medicare reimbursement is insufficient to cover the costs of certain therapeutics that treat patients with rare diseases, a disincentive can be created in addressing these conditions."[21] ARM greatly appreciates the inherent conflict that exists with certain potential solutions. Because MS–DRGs are a classification system intended to group together diagnoses and procedures with similar clinical characteristics and utilization of resources, MS-DRGs cannot work well for rare disease treatments.[22] Rare diseases, by definition, are conditions that are represented by low volumes in CMS' claims data thereby posing a unique challenge to the MS-DRG methodology, which relies on the law of averages as these conditions affect small subsets of the population.

To resolve this conflict, ARM urges CMS to develop a policy that prioritizes beneficiary access to rare disease therapies over historical approaches to MS-DRG development or integration of the rare disease therapy into the MS-DRG. As such, ARM recommends that CMS reimburse hospitals based on the Average Sales Price (ASP) methodology of the orphan drug as published in its HOPD Addendum B file.[23] CMS can implement this policy pursuant to §1886(d)(5)(I) that states "[t]he Secretary shall provide by regulation for such other exceptions and adjustments to

[20] 83 Fed. Reg. 41,144, 41,201 (August 17, 2018).
[21] 87 Fed. Reg. at 28,197.
[22] 87 Fed. Reg. at 28,195.
[23] In circumstances where ASP is not available, ARM urges CMS to reimburse hospitals based on WAC consistent with §1847A(c)(4)(A)(i).

such payment amounts under this subsection as the Secretary deems appropriate." This is the same authority that the Agency relied on to make the COVID payment adjustments. ARM believes that the reimbursing based on the ASP methodology will preserve access to the therapy, can be consistently applied, is transparent and is market based. Additionally, ASP reimbursement will eliminate some of the inconsistent charging practices by hospitals such that more hospitals, especially those in underserved areas, can provide access to orphan drugs. Further, by using the same methodology as the outpatient setting, CMS will remove reimbursement from the site of care treatment decision. ASP can also help hospitals meet their own transparency requirements, and therefore is the best option.

In the alternative, CMS can use the same authority, or the authority in §1886(d)(4) to implement other payment adjustments that promote beneficiary access to orphan drugs. Specifically, CMS can create cost band MS-DRGs like those that exist in the outpatient setting and then assign the orphan drug to the corresponding cost band MS-DRG based on the claims data from the NTAP period. ARM is concerned, however, that this policy does not provide enough transparency into pricing such that current charge compression and cost-to -charge ratio issues will remain.

Finally, CMS could create orphan drug-based MS-DRGs per MDC for assignment post NTAP. In other words, each MDC could have orphan-drug MS-DRGs that are more clinically coherent than the cost-based MS-DRGs. While more consistent with traditional MS-DRG construction, ARM is concerned that this policy does not solve the problem because too many therapies with different prices and treatment goals would share the same MS-DRG. As such, ARM urges CMS to reimburse hospitals based on the ASP methodology post NTAP.

Conclusion

ARM is confident that meaningful improvements in clinical outcomes and cost reduction can be accomplished through regenerative medicine technologies. ARM believes that the field of regenerative medicine has the potential to heal people and bend the health cost curve toward lower long-term costs and higher quality outcomes. This trend is already evidenced by several approved and marketed first-generation regenerative medicine products that are demonstrating both clinical and cost reduction value. Accordingly, we could substantially reduce overall healthcare expenses by reducing hospital care, the need for physician, clinical and professional services, nursing, and home healthcare.

ARM looks forward to working with CMS to further establish greater transparency and payment accuracy within the IPPS for all innovative treatments. ARM believes that these fundamental principles should serve as the foundation for the MS-DRG system that will continue to stimulate and reward innovation in the inpatient setting with further downstream positive impact on other payers such as Medicaid and private insurers.

We thank CMS for its many proposals and statements in the proposed rule and look forward to working with CMS to establish policies that promote appropriate access to regenerative medicine therapies in both the near term and long. Please feel free to contact Brett Logan at blogan@alliancerm.org with questions.

Sincerely,

Erica Cischke, MPH
Vice President, U.S. Government Affairs
Alliance for Regenerative Medicine

Appendix A:

Alliance for Regenerative Medicine

The below information reflects therapies that have known FDA designations outside of standard approval processes.

Please note:

- This list reflects publicly available information as of April 2023; indications, designations, and other factors may change over time.
- Line of therapy is not considered in the indications data.
- Original source and definitions from GlobalData Pharma Intelligence Center.

Approved Cell and Gene Therapies and Specific Approved Indications	Accelerated Approval	Break-through Therapy	Fast Track	Priority Review	RMAT	Orphan Drug	Rare Pediatric Disease	Number of Designations
Abecma		**X**		**X**		**X**		**3**
Refractory Multiple Myeloma		X		X		X		3
Relapsed Multiple Myeloma		X		X		X		3
Adstiladrin		**X**	**X**	**X**				**3**
Non Muscle Invasive Bladder Cancer		X	X	X				3
Breyanzi		**X**		**X**	**X**	**X**		**4**
Diffuse Large B-Cell Lymphoma		X		X	X	X		4
Follicular Lymphoma		X		X	X	X		4
Non-Hodgkin Lymphoma		X		X	X	X		4
Primary Mediastinal B-Cell Lymphoma		X		X	X	X		4
Carticel	**X**							**1**
Cartilage Degeneration	X							1
Carvykti		**X**		**X**		**X**		**3**
Refractory Multiple Myeloma		X		X		X		3
Relapsed Multiple Myeloma		X		X		X		3
Hemgenix		**X**		**X**		**X**		**3**
Hemophilia B (Factor IX Deficiency)		X		X		X		3
Kymriah	**X**	**X**		**X**	**X**	**X**	**X**	**6**
B-Cell Acute Lymphocytic Leukemia		X		X		X	X	4
Diffuse Large B-Cell Lymphoma		X		X		X		3
Follicular Lymphoma	X			X	X	X		4
Luxturna		**X**		**X**		**X**	**X**	**4**
Leber Congenital Amaurosis (LCA)		X		X		X	X	4
Retinitis Pigmentosa (Retinitis)							X	1
Omisirge		**X**		**X**		**X**		**3**
Hematopoietic Stem Cell Transplant		X		X		X		3
Rethymic		**X**		**X**	**X**	**X**	**X**	**5**
DiGeorge Syndrome		X		X	X	X	X	5
Skysona	**X**	**X**		**X**		**X**	**X**	**5**
Adrenoleukodystrophy (X-linked ALD)	X	X		X		X	X	5
Stratagraft				**X**	**X**	**X**		**3**
Burns				X	X	X		3
Tecartus	**X**	**X**		**X**		**X**		**4**
B-Cell Acute Lymphocytic Leukemia		X		X		X		3
Mantle Cell Lymphoma	X	X		X		X		4
Yescarta	**X**	**X**		**X**		**X**		**4**
Diffuse Large B-Cell Lymphoma		X		X		X		3
Follicular Lymphoma	X	X		X		X		4
Primary Mediastinal B-Cell Lymphoma		X		X		X		3
Zolgensma		**X**	**X**	**X**		**X**	**X**	**5**
Spinal Muscular Atrophy (SMA)		X	X	X		X	X	5
Zynteglo		**X**	**X**	**X**		**X**		**4**
Beta Thalassaemia		X	X	X		X		4
Unique Approved Therapies	**5**	**14**	**3**	**15**	**4**	**14**	**5**	**16**

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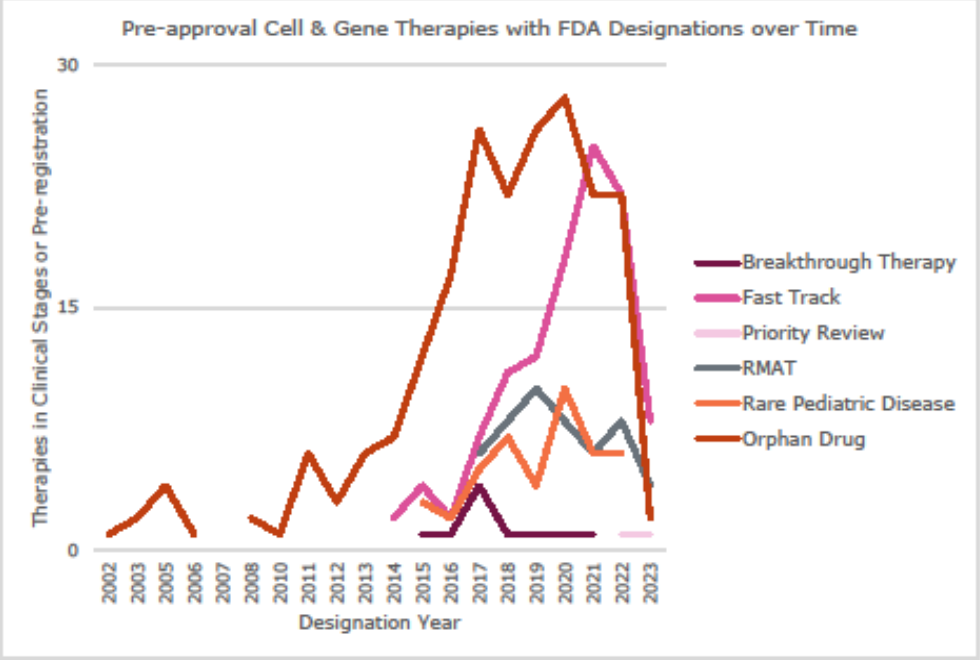
The below information reflects therapies that have known FDA designations outside of standard approval processes.

Please note:

- This list reflects publicly available information as of April 2023; indications, designations, and other factors may change over time.
- Pre-approval includes therapies with a clinical trial in phases 1-3 or pre-registration for a new drug or a new indication.
- Therapies may receive multiple designations or receive a designation across multiple years due to multiple indications.
- Original source and definitions from GlobalData Pharma Intelligence Center.



Designation Year	Designation Type						Number of Therapies Designated
	Breakthrough Therapy	Fast Track	Orphan Drug	Priority Review	Rare Pediatric Disease	RMAT	
2000-2010		2	11				**13**
2011-2015	1	7	34		3		**45**
2016-2020	8	50	119	1	28	32	**198**
2021-2023	1	55	46	2	12	18	**115**
2021	1	25	22		6	6	50
2022		22	22	1	6	8	49
2023 (Q1)		8	2	1		4	15
Number of Therapies Designated	**10**	**114**	**210**	**3**	**43**	**50**	**369**

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