DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF INSPECTOR GENERAL
WASHINGTON, DC 20201

[*We redact certain identifying information and certain potentially privileged, confidential, or proprietary information, unless otherwise approved by the requestor(s).*]

Issued: July 18, 2024

Posted: July 23, 2024

[Address block redacted]

Re: OIG Advisory Opinion No. 24-06 (Unfavorable)

Dear [redacted]:

The Office of Inspector General ("OIG") is writing in response to your request for an advisory opinion on behalf of [redacted] ("Requestor") regarding proposed financial support in the form of fertility services for eligible patients receiving [redacted] (the "Product"), a gene therapy product manufactured by Requestor (the "Proposed Arrangement"). Specifically, you have inquired whether the Proposed Arrangement, if undertaken, would constitute grounds for the imposition of sanctions under: the civil monetary penalty provision at section 1128A(a)(7) of the Social Security Act (the "Act"), as that section relates to the commission of acts described in section 1128B(b) of the Act (the "Federal anti-kickback statute"); the civil monetary penalty provision prohibiting inducements to beneficiaries, section 1128A(a)(5) of the Act (the "Beneficiary Inducements CMP"); or the exclusion authority at section 1128(b)(7) of the Act, as that section relates to the commission of acts described in the Federal anti-kickback statute and the Beneficiary Inducements CMP.

Requestor has certified that all of the information provided in the request, including all supplemental submissions, is true and correct and constitutes a complete description of the relevant facts and agreements among the parties in connection with the Proposed Arrangement. In issuing this opinion, we have relied on the facts and information Requestor presented to us and, in accordance with 42 C.F.R. § 1008.39(d), other publicly available information. This opinion is limited to the relevant facts Requestor presented to us, which we have not independently investigated, and the other publicly available information we reviewed in connection with our assessment of the Proposed Arrangement.

Based on the relevant facts certified in your request for an advisory opinion and supplemental submissions and the limited data available regarding, for example, the impact of fertility support on access to health care services; costs to Federal health care programs; patient outcomes; competition; and the risk of improper steering, we conclude that the Proposed Arrangement, if

undertaken: (i) would generate—if the requisite intent were present—prohibited remuneration under the Federal anti-kickback statute, which would constitute grounds for the imposition of sanctions under sections 1128A(a)(7) and section 1128(b)(7) of the Act; and (ii) would generate prohibited remuneration under the Beneficiary Inducements CMP, which would constitute grounds for the imposition of sanctions under the Beneficiary Inducements CMP and section 1128(b)(7) of the Act, as that section relates to the commission of acts described in the Beneficiary Inducements CMP.

As OIG has previously emphasized, an unfavorable advisory opinion does not prohibit the party or parties to whom the advisory opinion is issued from carrying out the arrangement or proposed arrangement that is the subject of the advisory opinion.[1] Importantly, where an unfavorable opinion relates to the application of the Federal anti-kickback statute, it is not a determination by OIG that the arrangement violates the Federal anti-kickback statute. Any such determination would require an assessment of intent, and OIG does not opine on intent as part of the advisory opinion process.

This opinion may not be relied on by any person[2] other than Requestor and is further qualified as set out in Part IV below and in 42 C.F.R. Part 1008.

I. FACTUAL BACKGROUND

A. The Product

Requestor is a pharmaceutical manufacturer that offers gene editing therapies for severe genetic diseases. Relevant to the Proposed Arrangement:

- The U.S. Food and Drug Administration ("FDA") has approved the use of the Product as a gene therapy for the treatment of [redacted] ("Condition A") in patients ages 12 and older. Condition A is the most severe form of [redacted]; patients are dependent on regular blood transfusions to avoid severe anemia and, when the patient is a child, debilitating developmental complications. Requestor certified that the Product is a one-time, potentially curative treatment for Condition A.[3]

- The FDA has approved the use of the Product as a gene therapy for the treatment of [redacted] ("Condition B") in patients ages 12 years and older with recurrent vaso-occlusive crises ("VOCs"). Condition B is a debilitating genetic blood disorder that affects the shape of the patient's blood cells and can make blood cells stickier than usual. When blood cells stick to one another, they can form clusters in the bloodstream. These clusters then block the flow of blood and oxygen, which can damage the blood vessels

[1] OIG, Advisory Opinion FAQs, https://oig.hhs.gov/faqs/advisory-opinion-faqs/.

[2] We use "person" herein to include persons, as referenced in the Federal anti-kickback statute and Beneficiary Inducements CMP, as well as individuals and entities, as referenced in the exclusion authority at section 1128(b)(7) of the Act.

[3] [Redacted]

and organs. These blockages can lead to VOCs. Requestor certified that the Product is a one-time, potentially curative treatment for Condition B.[4]

The list price of the Product is over $2 million. There are multiple treatment stages for Condition A and Condition B patients who are treated with the Product. Patients first must undergo one or more consultations with a physician at a hospital treatment center approved by Requestor ("Treatment Center") to determine eligibility for treatment with the Product. When a physician determines treatment with the Product is clinically appropriate, and the patient (or the patient's caregiver(s)) elects to move forward with such treatment, then the physician prescribes the Product for the patient and subsequently oversees the patient's entire treatment program. In addition to determining eligibility and overseeing treatment, the treating physician manages the patient's medical care throughout treatment and recovery, in consultation with a Treatment Center's care team. As part of the treatment regimen but prior to treatment with the Product, Condition A and Condition B patients must undergo chemotherapy-based fully-myeloablative conditioning ("Conditioning"), which clears existing stem cells from the bone marrow so they can be replaced with the edited cells. Conditioning can result in significant side effects, including infertility.

Requestor certified that there is one alternative gene therapy treatment to the Product available for Condition A and Condition B patients. Other than gene therapies, the only other established, curative treatment for Condition A and Condition B is hematopoietic stem cell transplant; however, the availability of stem cell donors is limited. Conditioning is also required for hematopoietic stem cell transplant. There is ongoing research that may: (i) expand the availability of hematopoietic stem cell transplant; and (ii) lessen the side effects from Conditioning, which would potentially benefit Condition A and Condition B patients.[5]

B. The Proposed Arrangement

Under the Proposed Arrangement, Requestor would provide financial support, up to a maximum of $70,000, for fertility services, including patient counseling, fertility drugs, collection and storage of oocytes or sperm, genetic testing, intrauterine insemination, and in-vitro fertilization procedures, as applicable to the individual patient, to eligible male and female patients, including Federal health care program enrollees, who are prescribed the Product and whose insurance does not cover fertility services. According to Requestor, the Proposed Arrangement would assist patients who may otherwise forgo treatment because of the risk of infertility associated with the Product and their inability to afford fertility services. Requestor would utilize a vendor to coordinate the fertility services (the "Fertility Vendor"). The Fertility Vendor would assist eligible patients and their caregiver(s) (for patients under the age of 18) by identifying fertility services providers. Patients and their caregivers would select their fertility providers and treatments; neither Requestor nor the Fertility Vendor would select the fertility providers or treatments, and Requestor would not receive any information about the selected fertility providers or treatments. The Fertility Vendor would pay fertility providers for the fertility

[4] [Redacted]

[5] [Redacted]

services provided to patients, and neither Requestor nor the Fertility Vendor would make any payments to patients or their caregivers for fertility services.

Requestor certified that its employees would provide non-promotional information to Treatment Centers about the Proposed Arrangement (e.g., patient eligibility criteria) using materials and messages approved by the company's internal review procedures. Requestor certified that it would not use the Proposed Arrangement as a marketing tool to drive product selection, utilization, or referrals.

The Proposed Arrangement would be available to patients who: (i) reside in the United States or a U.S. territory; (ii) have an annual household income at or below 670 percent of the Federal Poverty Level; (iii) are prescribed the Product for an on-label indication; and (iv) have insurance coverage that does not include fertility services. Moreover, Requestor would require patients (or their caregiver(s)) to acknowledge and agree that they would not seek reimbursement from any insurance provider or other third-party source for fertility services paid for by Requestor.

II. LEGAL ANALYSIS

A. Law

1. Federal Anti-Kickback Statute

The Federal anti-kickback statute makes it a criminal offense to knowingly and willfully offer, pay, solicit, or receive any remuneration to induce, or in return for, the referral of an individual to a person for the furnishing of, or arranging for the furnishing of, any item or service reimbursable under a Federal health care program.[6] The statute's prohibition also extends to remuneration to induce, or in return for, the purchasing, leasing, or ordering of, or arranging for or recommending the purchasing, leasing, or ordering of, any good, facility, service, or item reimbursable by a Federal health care program.[7] For purposes of the Federal anti-kickback statute, "remuneration" includes the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind.

The statute has been interpreted to cover any arrangement where one purpose of the remuneration is to induce referrals for items or services reimbursable by a Federal health care program.[8] Violation of the statute constitutes a felony punishable by a maximum fine of $100,000, imprisonment up to 10 years, or both. Conviction also will lead to exclusion from Federal health care programs, including Medicare and Medicaid. When a person commits an act described in section 1128B(b) of the Act, OIG may initiate administrative proceedings to impose civil monetary penalties on such person under section 1128A(a)(7) of the Act. OIG also may

[6] Section 1128B(b) of the Act.

[7] Id.

[8] E.g., United States v. Nagelvoort, 856 F.3d 1117 (7th Cir. 2017); United States v. McClatchey, 217 F.3d 823 (10th Cir. 2000); United States v. Davis, 132 F.3d 1092 (5th Cir. 1998); United States v. Kats, 871 F.2d 105 (9th Cir. 1989); United States v. Greber, 760 F.2d 68 (3d Cir. 1985).

initiate administrative proceedings to exclude such person from Federal health care programs under section 1128(b)(7) of the Act.

2. Beneficiary Inducements CMP

The Beneficiary Inducements CMP provides for the imposition of civil monetary penalties against any person who offers or transfers remuneration to a Medicare or State health care program beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier for the order or receipt of any item or service for which payment may be made, in whole or in part, by Medicare or a State health care program. OIG also may initiate administrative proceedings to exclude such person from Federal health care programs. Section 1128A(i)(6) of the Act defines "remuneration" for purposes of the Beneficiary Inducements CMP as including "transfers of items or services for free or for other than fair market value." Section 1128A(i)(6) of the Act contains an exception to the definition of "remuneration" that may apply in the context of the Proposed Arrangement. Section 1128A(i)(6)(F) of the Act provides that, for purposes of the Beneficiary Inducements CMP, the term "remuneration" does not include "remuneration which promotes access to care and poses a low risk of harm to patients and Federal health care programs (as defined in section 1128B(f) and designated by the Secretary under regulations)" (the "Promotes Access to Care Exception"). We have interpreted this provision to apply to:

> [i]tems or services that improve a beneficiary's ability to obtain items and services payable by Medicare or Medicaid, and pose a low risk of harm to Medicare and Medicaid beneficiaries and the Medicare and Medicaid programs by—(i) [b]eing unlikely to interfere with, or skew, clinical decision making; (ii) [b]eing unlikely to increase costs to Federal health care programs or beneficiaries through overutilization or inappropriate utilization; and (iii) [n]ot raising patient safety or quality-of-care concerns . . . .[9]

B. Analysis

As we explain in greater detail below, OIG has concluded that it lacks sufficient data to determine that the Proposed Arrangement is sufficiently low risk to issue a favorable advisory opinion at this time.

We recognize that cell and gene therapies consist of an evolving field that holds significant promise for improving the health of patients, including Federal health care program enrollees. Indeed, we understand that cell and gene therapies, like the Product, can transform the lives of individuals living with Condition A and Condition B. The number of cell and gene therapies that are available in the marketplace is rapidly increasing; payors, clinicians, and other stakeholders are adapting to the proliferation of these innovative therapies (e.g., paying for and providing these treatments).[10] These treatments are novel, and much is yet unknown about them and

[9] 42 C.F.R. § 1003.110 (defining "remuneration").

[10] See, e.g., Medicaid and CHIP Payment and Access Commission, Payment and Coverage of High-Cost Specialty Drugs Report from Technical Advisory Panel (Jan. 2021),

optimal arrangements for ensuring appropriate access to them. This uncertainty makes it difficult to assess the risk of the Proposed Arrangement and offer prospective immunity under our fraud and abuse authorities.

As these transformative therapies become available to patients and the marketplace for them evolves, we expect additional data to become available regarding the ability of Federal health care program enrollees to access these important treatments, as well as data regarding costs, benefits, risks, and outcomes of treatments. Illustratively, we expect additional data related to the provision of fertility services by a pharmaceutical manufacturer at no cost to Medicaid enrollees who receive gene therapy treatments from the Cell and Gene Therapy Access Model developed by the Center for Medicare and Medicaid Innovation ("Innovation Center") at the Centers for Medicare & Medicaid Services ("CMS"). As more data become available, we may consider them in future risk assessments regarding arrangements similar to the Proposed Arrangement.

Nothing in this opinion forecloses CMS from testing a model that includes fertility services through the Innovation Center, including through the Cell and Gene Therapy Access Model.[11] Safe harbor protection is available for CMS-sponsored model arrangements and CMS-sponsored model patient incentives, as set forth at 42 C.F.R. § 1001.952(ii). Moreover, nothing in this opinion addresses fertility services that are covered by a Federal health care program and nothing in this opinion impacts arrangements for patients who are uninsured or have private insurance.

1. Federal Anti-Kickback Statute

The Proposed Arrangement would implicate the Federal anti-kickback statute in two ways. First, the Proposed Arrangement would constitute remuneration to patients—including Federal health care program enrollees—that may induce them to purchase the Product. In particular, the Proposed Arrangement would cover up to $70,000 in fertility services, including patient counseling, fertility drugs, collection and storage of oocytes or sperm, genetic testing, intrauterine insemination, and in-vitro fertilization procedures. Further, Requestor explained that the Proposed Arrangement would assist patients who would otherwise forgo treatment because of the risk of infertility associated with Product treatment and their inability to afford fertility services. If a reason a patient would not receive treatment with the Product is the patient's inability to pay the costs associated with fertility services, then the Proposed Arrangement would address that inability to pay for these costs and likely would influence the patient's purchasing decision in connection with the Product. Consequently, the Proposed Arrangement would be designed to remove a financial barrier so that eligible patients would purchase the Product.

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https://www.macpac.gov/publication/payment-and-coverage-of-high-cost-specialty-drugs-report-from-technical-advisory-panel/.

[11] See, e.g., CMS, Cell and Gene Therapy (CGT) Access Model, https://www.cms.gov/priorities/innovation/innovation-models/cgt. While sickle cell disease is the initial focus of the model, CMS has indicated that additional cell and gene therapies for other diseases may be included in the model in the future.

Second, the Proposed Arrangement would constitute remuneration to the Treatment Centers and the treating physicians in the form of the opportunity to earn fees related to treatment with the Product (for patients—including Federal health care program enrollees—who otherwise would forgo treatment but for the Proposed Arrangement), which could induce Treatment Centers to recommend the Product and physicians to order the Product, as opposed to competitor drugs or other clinically appropriate treatments. No safe harbor would apply to the streams of remuneration resulting from the Proposed Arrangement.

As explained in greater detail above, in connection with the Proposed Arrangement, OIG currently lacks data to evaluate the factors OIG considers when assessing the risk of fraud and abuse under the Federal anti-kickback statute (e.g., increased or decreased access to health care services; increased or decreased costs to Federal health care programs; improved or worsened patient outcomes; competitive effects; and the risk of improper steering) and without such data, OIG cannot conclude at this time that the Proposed Arrangement would pose a sufficiently low risk of fraud and abuse under the Federal anti-kickback statute to grant prospective immunity. OIG's conclusion regarding the Proposed Arrangement does not impose any obligations on Requestor. This conclusion also is not a determination by OIG that the Proposed Arrangement would violate the Federal anti-kickback statute; it simply means that, in an exercise of its enforcement discretion, OIG declines to offer prospective immunity—through a favorable advisory opinion—to the Proposed Arrangement.

2. Beneficiary Inducements CMP

Under the Beneficiary Inducements CMP, we analyze whether Requestor knows or should know that the Proposed Arrangement would be likely to influence a beneficiary's selection of a particular provider, practitioner, or supplier for the order or receipt of any item or service for which payment may be made, in whole or in part, by Medicare or a State health care program. The facts here implicate the Beneficiary Inducements CMP because Treatment Centers and physicians practicing at Treatment Centers are providers and suppliers that recipients of the Proposed Arrangement could be induced to select.

Requestor's offer of the Proposed Arrangement valued at up to $70,000 constitutes remuneration to eligible patients, including State health care program beneficiaries. This valuable remuneration is likely to influence patients and Requestor should know that patients likely would be influenced to select a Treatment Center and a physician practicing at a Treatment Center over other providers and suppliers that are outside the Proposed Arrangement because, as Requestor certified, the Proposed Arrangement would assist patients who would otherwise forgo treatment because of the risk of infertility associated with the Product and their inability to afford fertility services. For the foregoing reasons, unless an exception applies, the Proposed Arrangement would generate prohibited remuneration under the Beneficiary Inducements CMP.

At this time, we conclude that neither the Promotes Access to Care Exception nor any other exception would be available to protect the Proposed Arrangement. We reach this conclusion because we lack data that would allow us to determine that providing the Proposed Arrangement to eligible patients improves the ability of patients to access the Product. It is possible that with time such data may become available and OIG could potentially make the determination that the Proposed Arrangement would constitute "[i]tems or services that improve a beneficiary's ability

to obtain items and services payable by Medicare or Medicaid" for the purposes of the Promotes Access to Care Exception. However, due to the lack of available data, we cannot conclude that the Proposed Arrangement would improve the patient's ability to obtain Federally reimbursable items or services for the purposes of this exception.[12]

No other exception to the Beneficiary Inducements CMP applies and the Proposed Arrangement would generate prohibited remuneration under the Beneficiary Inducements CMP. There is no exception that unconditionally protects the offer or provision of remuneration to individuals with financial need. We have long emphasized that "there is no meaningful statutory basis for a broad exemption based on the financial need of a category of patients . . . [and] that categorical financial need is not a sufficient basis for permitting valuable gifts."[13] The financial need requirement here similarly does not resolve the lack of data available to OIG to appropriately assess the fraud and abuse risks of the Proposed Arrangement.

III. CONCLUSION

Based on the relevant facts certified in your request for an advisory opinion and supplemental submissions and the limited data available regarding, for example, the impact of fertility support on access to health care services; costs to Federal health care programs; patient outcomes; competition; and the risk of improper steering, we conclude that the Proposed Arrangement, if undertaken: (i) would generate—if the requisite intent were present—prohibited remuneration under the Federal anti-kickback statute, which would constitute grounds for the imposition of sanctions under sections 1128A(a)(7) and section 1128(b)(7) of the Act; and (ii) would generate prohibited remuneration under the Beneficiary Inducements CMP, which would constitute grounds for the imposition of sanctions under the Beneficiary Inducements CMP and section 1128(b)(7) of the Act, as that section relates to the commission of acts described in the Beneficiary Inducements CMP.

As OIG has previously emphasized, an unfavorable advisory opinion does not prohibit the party or parties to whom the advisory opinion is issued from carrying out the arrangement or proposed arrangement that is the subject of the advisory opinion. Importantly, where an unfavorable opinion relates to the application of the Federal anti-kickback statute, it is not a determination by OIG that the arrangement violates the Federal anti-kickback statute. Any such determination would require an assessment of intent, and OIG does not opine on intent as part of the advisory opinion process.

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[12] As with any exception to the Beneficiary Inducements CMP, one element of an exception is not more important than any other element; all must squarely be satisfied to meet the applicable exception.

[13] OIG, Special Advisory Bulletin: Offering Gifts and Other Inducements to Beneficiaries (2002), http://oig.hhs.gov/fraud/docs/alertsandbulletins/SABGiftsandInducements.pdf.

IV. LIMITATIONS

The limitations applicable to this opinion include the following:

- This advisory opinion is limited in scope to the Proposed Arrangement and has no applicability to any other arrangements that may have been disclosed or referenced in your request for an advisory opinion or supplemental submissions.

- This advisory opinion is issued only to Requestor. This advisory opinion has no application to, and cannot be relied upon by, any other person.

- This advisory opinion may not be introduced into evidence by a person or entity other than Requestor to prove that the person or entity did not violate the provisions of sections 1128, 1128A, or 1128B of the Act or any other law.

- This advisory opinion applies only to the statutory provisions specifically addressed in the analysis above. We express no opinion herein with respect to the application of any other Federal, State, or local statute, rule, regulation, ordinance, or other law that may be applicable to the Proposed Arrangement, including, without limitation, the physician self-referral law, section 1877 of the Act (or that provision's application to the Medicaid program at section 1903(s) of the Act).

- This advisory opinion will not bind or obligate any agency other than the U.S. Department of Health and Human Services.

- We express no opinion herein regarding the liability of any person under the False Claims Act or other legal authorities for any improper billing, claims submission, cost reporting, or related conduct.

This opinion is also subject to any additional limitations set forth at 42 C.F.R. Part 1008. OIG reserves the right to reconsider the questions and issues raised in this advisory opinion and, where the public interest requires, to rescind, modify, or terminate this opinion.

Sincerely,

/Susan A. Edwards/

Susan A. Edwards
Assistant Inspector General for Legal Affairs