Science commentary explores ways to pay for success in gene therapy

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Stuart Orkin, M.D., Dana-Farber/Boston Children's Cancer and Blood Disorders Center. Credit: Dana-Farber/Boston Children's

As a new generation of gene therapy clinical trials shows promise to cure or halt the progression of several rare diseases, the time has come to explore ways to pay for the cutting edge treatments, a pediatric hematologist-oncologist from Dana-Farber/Boston Children's Cancer and Blood Disorders Center argues in a commentary published today by the journal *Science*.

Noting the potential of gene therapy to be a one-time treatment for rare and serious diseases that otherwise cost hundreds of thousands, if not millions, of dollars in chronic care over a lifetime, Stuart Orkin, MD, and co-author Philip Reilly, MD, JD, of Third Rock Ventures, seek to "catalyze the discussion" by suggesting several new models for valuing, pricing and developing gene therapy. The authors expect the federal Food and Drug Administration (FDA) will approve at least one gene therapy treatment within the next three years. Their suggestions include:

- Placing a high value on therapies that are expensive to develop and deliver, but ultimately cost less over the long-term than current treatment. For instance, treating a single hemophilia patient can cost $300,000 a year or $5 million -$10 million over a lifetime. Medical support for a single patient with sickle cell disease can run $25,000 a year or $1 million over a lifetime.
- "Tying costs to efficacy" by having pharmaceutical companies accept a "large initial up-front payment with lower periodic payments made annually so long as the therapy remains efficacious."
- Creating a federal initiative to support development of new therapies for ultra-rare diseases occurring in fewer than one in 250,000 births annually.
- Allowing some of the economic benefit derived from the Orphan Drug Act to be used to lower the price of new gene therapy drugs.
- Streamlining the regulatory process for developing genetic and

other treatments for rare diseases, recognizing the time-consuming difficulty of acquiring a critical mass of patients for clinical trials for disorders affecting very few people.

"It takes a long time to develop new genetic therapies, and it's a huge investment," says Orkin, who is also chairman of pediatric oncology at Dana-Farber Cancer Institute, associate chief of hematology-oncology at Boston Children's Hospital and professor of pediatrics at Harvard Medical School. "Once the FDA approves these therapies, they're going to have to be paid for. The sustainability of the whole industry depends on some kind of compensation in which companies realize a profit."

Initial gene therapy efforts suffered serious setbacks in the 1990s when patients in several clinical trials developed treatment-related leukemia and a young man in another trial died from his treatment. More recent clinical trials in a number of disorders - including immunodeficiencies, hemophilia, congenital blindness, thalassemia and metachromatic leukodystrophy - are showing promise of being both safe and effective. While the intent in most cases is cure, it is too early to know whether retreatment might be needed.

The pricing of gene therapy, the authors suggest, will be determined by the manner in which it is delivered, development and drug production costs and the size of the treatable population. The process of developing a new gene therapy treatment and securing FDA approval, they estimate, entails about eight years and direct costs of hundreds of millions of dollars.

"We recognize that there are many other approaches [to pay for gene therapy] that thoughtful study might uncover," the authors conclude, "but we need to begin to ensure that economic challenges are given the attention they deserve."

Boston Children's Hospital has offered non-exclusive licenses to for-profit entities on a patent developed by Orkin's laboratory regarding BCL11A, a genetic switch regulating hemoglobin production that is expected to form the basis of clinical trials for gene therapy and gene editing for sickle cell disease and thalassemia.

More information: *Science* science.sciencemag.org/cgi/doi … 1126/science.aaf4770

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