Molecular Therapy
Letter to the Editor

Financial considerations in expanded access policy for gene therapies: A tough nut to crack?

To the editor:

We wholeheartedly support the message by Kearns et al.[1] that "gene therapy companies have an ethical obligation to develop expanded access policies." The authors discuss several important factors that companies should consider when developing expanded access policies: clinical trial design, potential for data collection, risk-benefit analysis, and impact on program feasibility and profitability. Although the authors point to the costs of running expanded access programs, there is an additional financial argument specific to gene therapies that requires further attention.

Gene therapies are often single-dose, potentially curative treatments developed for patients with rare or ultra-rare diseases. With a (very) limited patient population, providing expanded access free of charge will eat away at the future commercial potential of the treatment. This is an important consideration in discussions of expanded access to gene therapies. It only applies to (ultra-)rare indications, where providing expanded access to "a handful of patients" may be equivalent to several percentage points of the entire patient population. Clearly, the relative impact of providing free-of-charge product in expanded access diminishes as the patient population increases. However, the one-off, potentially curative nature of (pediatric) gene therapies renders expanded access to such therapies fundamentally different from expanded access to longer-duration or chronic treatments and raises serious questions about feasibility and profitability.

In developing policies for expanded access, manufacturers are caught between shareholders and societal responsibilities. Withholding access to gene therapies because of financial motivations would not generate sympathy among patients, patient organizations, and the general public. But on the other hand, a return on investment would ensure development and innovation of gene therapies for future patients, and the latter, ethically, is worth striving for. Although reimbursement for unapproved treatments is procedurally problematic for insurance companies or national health services, companies may need to be compensated for the high cost specifically associated with administering and manufacturing gene therapies to avoid direct losses. Alternative reimbursement schemes and the involvement of public payers might provide a solution to this problem. Indeed, innovative ways of reimbursement have been proposed and implemented for gene therapies.[2] For example, "pay-for-performance" schemes incorporate outcome-based payments to share the risk of variability in (long-term) outcomes between payers and the industry.[3] Finally, we agree with the authors' previous arguments that, at a minimum, acceptance of data from patients treated under expanded access in regulatory decision making may help incentivize companies to arrange for expanded access.[4,5]

Given the certain high prices of gene therapies and the uncertain long-term cost effectiveness, aligning societal and industry perspectives on expanded access to gene therapies remains "a tough nut to crack." The authors deserve credit for their efforts to advance the field of the ethics of expanded access in general, and that of pediatric gene therapies in particular. We hope that their work and the above considerations may positively impact manufacturers' decisions to provide expanded access. Either way, we fully agree with Kearns et al.[1] that expanded access policy should be transparently explained and publicly accessible.

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https://doi.org/10.1016/j.ymthe.2021.04.030

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