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EDITORIAL

Gene Therapy, more than ever—a new vision for the journal

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Gene Therapy has been a partner in the development of the genetic and cellular therapeutics field from 1994. For most of that time, over 20 years, Joe Glorioso and Nick Lemoine have been at the helm, leading the journal, ensuring it stayed in the mainstream and helping shape critical developments. In their farewell editorial in this issue they review their experience and outline the progress, challenges and their faith in the therapeutic potential of the field. Last January I was honoured to take over as Editor-in-Chief, and in this editorial introducing the *Spinraza and Advanced Therapies: a stakeholder special* issue of *Gene Therapy* I aim to both outline and showcase the new vision for the journal.

Since the journal was founded, society as a whole has changed in many respects. Globalization, the internet, social media, community stakeholders, gender equality, empowerment, inclusion and outreach have become critical to the success of our scientific activity, as they have for every other human endeavour. We all have strived to understand these new concepts and taken steps, sometimes shyly, to assimilate them. In this new era for *Gene Therapy*, our aim is to embrace the opportunities that society offers and demonstrate that we can lead by example for the progress of our field.

Gene Therapy is welcoming a new editorial team who will work together in the delivery of this vision. Our global reach will be supported by Associate Editors Patrick Harrison (Europe), Qiurong Ding (Asia), Ursula Matte (South America), Patrick Arbuthnot (Africa), Marguerite Evans-Galea (Australasia) and a North America Associate Editor yet to be appointed (expressions of interest addressed to me at editor e-mail address below are encouraged). Manuscript handling will be non-geographical, but each editor will strive to promote the journal's aims in their area of influence and expertise. We will do this in unison with the deployment of brand-new internet-based tools: our new responsive website, and the Facebook, Instagram and Twitter accounts handled by Social Media Editor Versha Prakash. We are supported by Editorial Assistant Jaspreet Nijjar (answering at genetherapy@nature.com) and Publishing Editor Virginia Boylan.

The *Spinraza and Advanced Therapies: a stakeholder special* issue that follows in the next pages aims to highlight the Spinraza (nusinersen) breakthrough and the importance of involving all stakeholders for the successful development of therapeutics, the latter being a central theme of the vision that we promote. Spinraza, the first drug approved for the treatment of spinal muscular atrophy (SMA), is a real trailblazer for rare disease. Technically, Spinraza is an antisense oligonucleotide and thus not classed as a gene therapy in the US or an advanced therapy medicinal product (ATMP) in the EU. However, the mechanism of action of Spinraza is based on a thorough understanding of the molecular basis of SMA and shows how genetic therapies can be rationally designed when significant knowledge about the disease has been gathered. In addition, SMA is a severe disease with a relatively high incidence, estimated between 1:6000 and 1:10 000 live births. The availability of Spinraza, a treatment with broad label, impacts a large number of people, from babies and infants through to adults. It also has implications for the possible introduction of newborn screening and showcases the difficulty in providing affordable access to advanced treatments. After an editorial on the topic by Versha Prakash, this special issue covers a variety of perspectives and includes comments and review papers from SMA research funders, people affected, experts in the advanced therapies field, SMA scientists and clinicians, regulators, ethics and pricing/IP experts, and community stakeholders. Going beyond Spinraza, the issue covers genomics projects for personalised medicine, the importance of international collaboration in rare disease research, showcases on-going research in Asia, South America and Africa, and provides academic and corporate perspectives on the delivery of advanced therapies. It also includes a compilation of online resources of relevance. Overall this content shows the global, inclusive and accessible way in which we want to develop the journal. We will welcome content from all stakeholders, on occasion publish controversial opinion pieces and in all cases do our best to uphold scientific standards. To encourage an artistic perspective to our scientific activity, we have started publishing cover images and will seek and welcome artistic content similar to what is on the cover of this issue.

These are exciting times to work in gene and cell therapy, as attested by the marketing approval of a small but growing number of gene and cell therapies, and the increasing involvement of the pharmaceutical industry. Autologous, CD19-directed chimeric antigen receptor T-cells (CAR-T cells, marketed as Kymriah and currently approved for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse), have become the first US gene and cell therapy product, and importantly have been developed with global market logistics. The prospects of gene editing and stem cell treatments are also highly encouraging. However, we are acutely aware of two critical issues that need addressing. One is the imbalance between the ability to diagnose and to treat disorders, particularly for rare disease, where genomic diagnostics have become extremely effective compared to the scarcity of therapies. This imbalance highlights the complexity of therapy development and can only be improved by targeting resources, as has been done to encourage the development of genomic technologies. Governments, other research funders, industry and all stakeholders must find constructive ways to promote technology development in the therapeutic area as a priority if this gap is to be reduced. This must be coupled to streamlined approval processes for advanced therapies.

The second issue of concern is the provision of access to marketed treatments for affected people. Across the field, particularly for rare disease, target identification, pre-clinical and, in some cases, even initial clinical development are often carried out by academic labs with charity and/or government funding. Pharma often becomes involved at a relatively late stage and hence provides limited investment. Despite this, huge list prices have been set for marketed viral vectors (Glybera, €1 000 000+ for one-off dosing), genetically modified stem cells (Strimvelis, €594 000 for one-off dose) or antisense oligonucleotides (Spinraza, $125 000 in USA or €90 000 in EU per dose, at 6 doses in the first year and 3 per year thereafter), which are neither affordable nor sustainable. Spinraza is a relatively simple chemical molecule that can be synthesised at a fraction of the cost required to produce viral vectors or genetically modified cells. However, the initial list prizes of Spinraza give the impression that production costs are relatively irrelevant when prices are set and have been a disappointment for many stakeholders. A variety of novel pricing

and reimbursement strategies must be found, as access to and funding of healthcare are very different across the world, and the number of people affected by various diseases ranges enormously. Pricing and marketing must be based on ethical principles, with the ultimate goal of maximising access in a profitable (ideally altruistic) manner, rather than maximising profit at the expense of access. Big pharma has a critical role to play and must hold its nerve through such complex development and marketing. In the end, therapeutic tools developed in the rare disease area will be applied to common diseases, where more attractive investment returns will be available.

Finally, *Gene Therapy* is a scientific journal and our core goals must include publishing high-quality material and reaching as wide a reader base as possible. We will make some changes to our Aims&Scope to reflect the expansion of our field, and appoint a new editorial board to support the team of editors. We will strive to attract the best science and provide an excellent experience for our authors. We will explore options to improve full access to our content and will support our authors to maximise dissemination of their work. We want authors to be proud of publishing in *Gene Therapy* and readers to seek our content, with the ultimate goal of contributing to the development of advanced therapies for the benefit of affected people.

CONFLICT OF INTEREST

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