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► **COVER:** 'Improving R&D productivity' by Susanne Harris, inspired by the Analysis on p203.

The rising cost of drug research and development (R&D), coupled with patent expirations on blockbuster products and increasingly cost-constrained health-care systems, are posing unprecedented challenges to the future viability of the pharmaceutical industry.

In their Analysis article, Paul and colleagues argue that improving R&D productivity is the key to addressing these challenges. By constructing an economic model of each phase of drug discovery and development using recent industry-wide data, they identify the major contributors to escalating R&D costs and use this as a basis to present strategies to improve the efficiency of drug R&D. Two further articles also consider challenges faced in drug development programmes. First, the importance of the effects of membrane transporters on drug pharmacokinetics, safety and efficacy is increasingly being appreciated. A comprehensive report from the International Transporter Consortium summarizes the roles of key membrane transporters in drug disposition and response, discusses methods for evaluating their impact and presents decision trees to help guide clinical studies. The second article focuses on advanced therapy medicinal products (ATMPs), such as gene and cell-based therapies, for which there are several issues hampering their clinical development. In their Perspective, the European Committee for Advanced Therapies discuss their regulatory role at the European Medicines Agency, presenting common challenges faced in ATMP development, and approaches and opportunities to address them. Finally, Aguzzi and O'Connor review recent progress in understanding the common structural and pathogenic features of diverse protein aggregation disorders, including Alzheimer's disease, systemic amyloidoses and prion diseases. Promising therapeutic approaches aimed at preventing or reversing pathological protein aggregation are also highlighted.



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