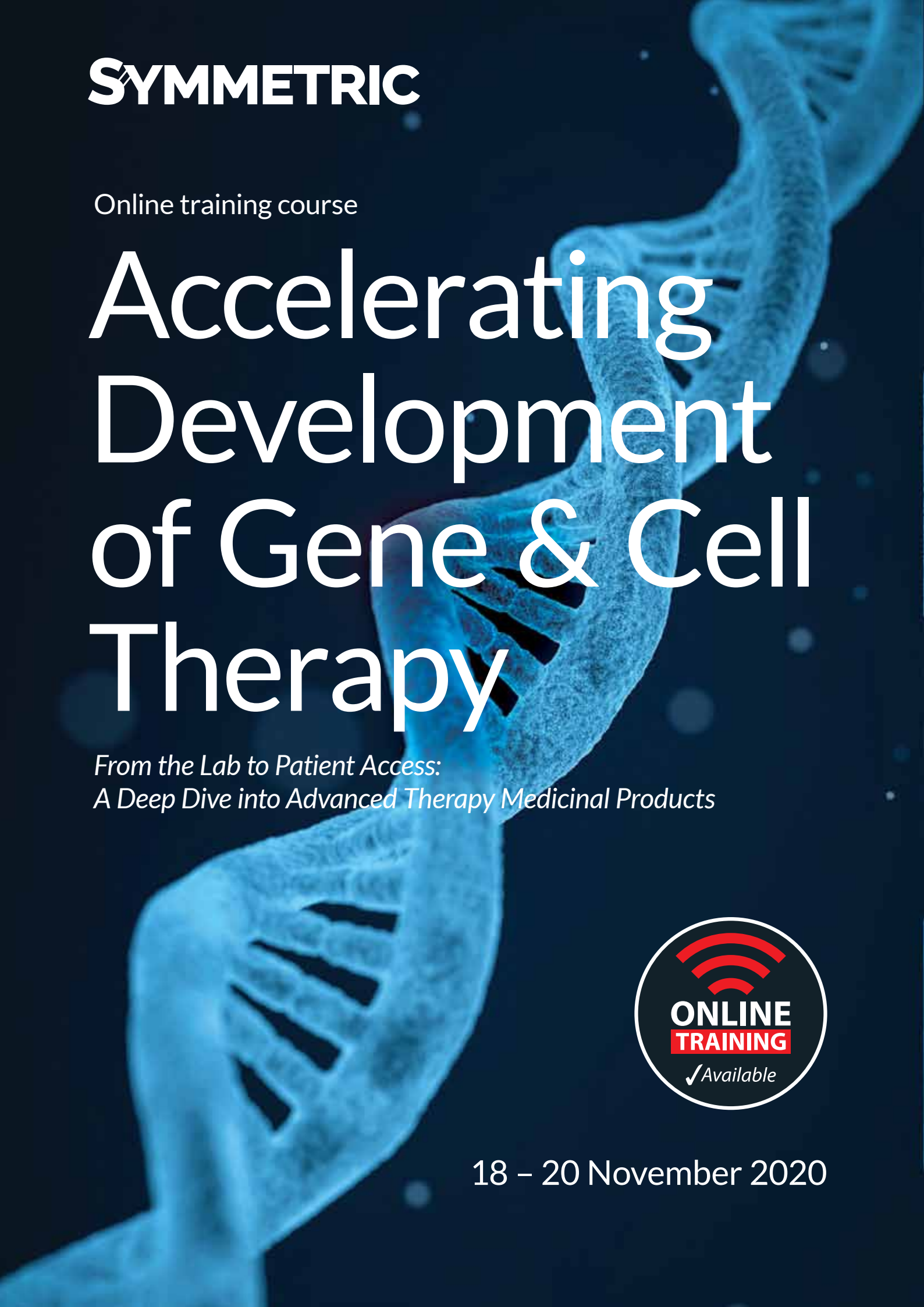
SYMMETRIC

Online training course

Accelerating Development of Gene & Cell Therapy

From the Lab to Patient Access:
A Deep Dive into Advanced Therapy Medicinal Products



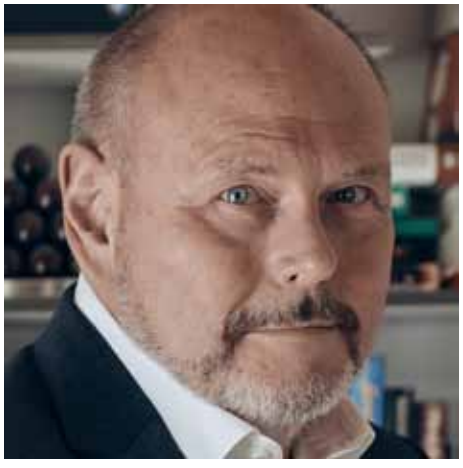
18 – 20 November 2020

Course description

This unique training focuses on methods enabling to leverage patient engagement, novel rare disease trial designs, regulatory incentives and real-world evidence to accelerate the development, approval and patient access of innovative Advanced Therapy Medicinal Products (ATMPs), including autologous and allogeneic gene therapies, tissue engineered products and somatic cell therapies.

Your Trainer

David Schwicker
ORPHA Strategy Consulting
CEO



Key topics

- An Introduction to Advanced Therapy Medicinal Products
- Accelerated Development Strategy for ATMPs
- "Fast to Patient" Regulatory Strategy
- ATMPs Pricing and Market Access
- Gene Therapy Safety, Risk Evaluation
- ATMPs Interactive Case Studies

David Schwicker has biopharmaceutical consulting expertise spanning more than 25 years. Founder of ORPHA Strategy Consulting, and former Vice President with PAREXEL International in the United States, David is a sought-after expert for accelerating marketing authorisation, time to launch, early patient and market access in the hyper-dynamic environment of rare conditions, orphan and advanced therapy medicinal products. David's extensive therapeutic area experience includes acute myelogenous leukemia (AML), multiple myeloma (MM), cutaneous t-cell lymphoma (CTCL), non-small-cell lung cancer (NSCLC), breast cancer, neuroendocrine tumors, pulmonary arterial hypertension (PAH), Niemann Pick disease, acromegaly, graft versus host disease (GvHD), primary sclerosing cholangitis (PSC), Mucopolysaccharidosis (MPS), Myasthenia Gravis (MG), Graves Orbitopathy (GO), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Antibody-Mediated Organ Rejection (AMR), Leber's congenital amaurosis (LCA), retinitis pigmentosa (RP), USHER Syndrome, Narcolepsy, and Friedrich's ataxia. David is currently working in rare Inherited Retinal Dystrophies (IRD), oncology/hematology, metabolic, CNS and dermatological indications. David has developed a unique understanding of accelerating marketing authorization and market access for orphan drugs. This involves indication prioritization, evidence generation planning, patient engagement and PROs, orphan designation, compassionate use programs, product differentiation and early value demonstration with fewer data. A crucial component of early access strategy is the application of innovative pathways that leverage the use of real-world evidence (RWE). David is the author and co-author of numerous peer-reviewed publications and speaker at international meetings (ISPOR, RAPS EU Congress, Orphan Drugs Development and Commercialisation, Expanded Access Summit). He is an accomplished trainer in rare diseases, orphan, gene and cell therapy medicinal products, and leads training courses as well as customized in-house training workshops.

Cross Cutting Theme

- The 50-60 million individuals living with rare conditions represent a **huge unmet medical need**, which is often life-threatening, highly debilitating, requiring complex care and great urgency.
- The **cross-cutting theme** of this course is therefore **"fast to patient"**: the acceleration of discovery, development, authorisation, manufacturing and market access in order to ensure the timely access to potentially curative treatments.
- Successful development and commercialisation of Advanced Therapies requires the **integration of development, regulatory, manufacturing** and **market access strategies.**

The intersection point of these strategies is proposed as the joint vision of the earliest patient access.

Key takeaways

- ✓ **Explore** the opportunities of digital and big data to accelerate discovery, development, regulatory approval and market access
- ✓ **Gain** insight into the most recent methodologies for faster, smaller, smarter clinical trials, including Phase I/II studies that are robust enough for marketing application
- ✓ **Discuss** strategies to limit the number of patients and the placebo exposure of participants in pivotal clinical trials in rare and ultra-rare conditions
- ✓ **Discover** the newest regulatory approaches for gene and cell therapies
- ✓ **Consider** the crucial role of patient engagement throughout the ATMP lifecycle
- ✓ **Analyse** the current market access challenges for ATMPs as well as innovative strategies that integrate patient-centric real-world evidence

Who should attend?

- **Heads of R&D and global program leads**
- **Regulatory executives**
- **C-level executives, senior business development strategists, portfolio executives**
- **Experienced pricing and market access executives**
- **Medical affairs executives**
- **Marketing and commercial executives**
- **Finance executives**
- **Patient advocates**
- **Epidemiologists, outcomes researchers and health economists**
- **Digital health, Big data and RWE researchers**

Day 1

18 November 2020 | 14:00 - 18:00 CET, 8:00 - 12:00 EDT

MODULE 1: An Introduction to Advanced Therapy Medicinal Products

- What makes gene and cell therapies stand out: the enormous potential of "one and done" cures, commercial challenges
- Defining rare and ultra-rare conditions and the industry outlook to 2024
- Efficiency, ROI and investment in rare disease drug development
- Million-dollar cures and the affordability debate: hyper-personalized, hyper-accurate, hyper-expensive - who will have access?

MODULE 2: Accelerated Development Strategy

- Patient-centred research: transforming ATMP development and evidence generation
- Patient engagement objectives and ROI: identifying populations, faster clinical trials, incorporating patient-relevant endpoints (PROs), de-risking
- ATMP asset strategy, indication prioritisation, clinical planning and de-risking
- Drafting an ATMP Target Product Profile (TPP) and an Early Value Proposition (EVP)
- Biomarker (CDx) and digital health (DTx) based strategies: increased speed, decreased risk
- The specific challenges of preclinical research and CMC for ATMPs
- Integrating compassionate use and expanded access programs into rare development
- The randomised clinical trial (RCT) and real-world evidence (RWE) continuum: utilising the full evidence spectrum to accelerate development
- Clinical trials in small populations and rare diseases:
  single arm studies and external controls, precision medicine trials, N-of-1 trials, eINDs, exceptional responders, master protocols and platform trials, adaptive designs, randomised delayed start (RDS), RWE enrichment, randomised registry trials, pragmatic RCTs

Interactive Case Studies:

- PROs in labelling: haemophilia A, myelofibrosis, immuno-oncology
- Zalmoxis (somatic cell therapy) historical controls from the EBMT registry
- Kymriah (CAR T-cell therapy) preclinical program and CMC challenges
- Luxturna (adeno-associated viral vector - AAV - gene therapy) randomised delayed start trial design with real-world controls
- Platform trials: ISPY-2, Beat AML and Precision Promise (targeted oncology)
- Mepsevii (enzyme replacement therapy) N=1 "trial", expanded access (eIND) in MPSVII
- Strimvelis (ex-vivo autologous gene therapy) ultra-rare population registry (ADA-SCID)
- A natural history study in CLN2 (Batten) disease informs the pivotal study design and provides historical controls, enabling early FDA and EMA approval of Brinuera (enzyme replacement therapy)
- Uridine triacetate and Lutathera: leveraging RWD & RWE from expanded access
- Rettsyndrome.org: driving patient-led research forward

DAILY SCHEDULE

14:00 - 18:00 CET, 8:00 - 12:00 EDT **Daily Sessions**

Each daily session will contain two 15 min coffee breaks

Day 2

19 November 2020 | 14^{00} - 18^{00}

MODULE 3: "Fast to Patient" Regulatory Strategy

- Incentives for developers; special incentives for Small and Mid-Sized Corporations (SMEs)
- Accelerating submission and review timelines:
- FDA Expedited Programs in Serious Conditions
  - Regenerative Medicine Advanced Therapy Designation (RMAT)
  - Interact pre-pre IND Meetings and Fast Track designation (FT)
  - Breakthrough Therapy designation (BRT)
  - Accelerated Approval (AA)
  - Priority Review (PR)
- EMA's Support for Early Access: High Unmet Need and Transformative Treatments
  - Committee for Advanced Therapies (CAT): ATMP-specific legislation and support
  - Conditional Marketing Authorisation and Authorisation in Exceptional Circumstances
  - Paediatric Investigation Plans (PIP)
  - The PRIME Scheme: the ideal ATMP pathway?
  - Parallel consultations EMA and HTABs (via EUnetHTA)
- New (2020) gene therapy guidance: rare conditions, CMC/cGMP, long-term follow-up
- Addressing gene therapy safety, Risk Evaluation and Mitigation Strategies-(REMS)

Interactive Case Studies:

- ATMPs and PRIME: Kymriah and Yescarta (CAR T-cell therapies), the first products approved through the scheme
- Kymriah special protocol assessments, PIPs, regulatory interactions and timelines (FDA)
- Alofisel (darvadstrocel, human allogeneic mesenchymal adult stem cells), orphan designation and orphan exclusivity at marketing authorisation
- ATMP long-term follow up: 15-year follow-up registry in ADA-SCID for Strimvelis (ex-vivo autologous gene therapy), and EMA's & EUnetHTA's CAR T-cell therapy registries

"Fast to Patient" – Accelerating Development of Gene and Cell Therapy

Focussed clinical programs and **adaptive pathways** to bring treatments to patients in the most timely manner

Generating **patient-relevant outcomes** with sustained patient engagement throughout the life-cycle

Early value demonstration specifically addressing the challenges of early market access with fewer clinical data

Differentiated & value-based offerings with the greatest net benefit for successful pricing and reimbursement

Maximising product value from launch to LOE with a life-cycle full-spectrum evidence generation strategy

Addressing R&D efficiency and a hyper-competitive landscape with a **"fast to market" approach**

Day 3

20 November 2020 | 14:00 - 18:00 CET, 8:00 - 12:00 EDT

MODULE 4: ATMP Pricing and Market Access

- Accelerating and facilitating patient access to gene therapies - a major health care concern
- Market access and pricing & reimbursement (MA/P&R) challenges for ATMPs: high upfront costs, long-term uncertainties and the value assessment of potential cures
- Budget impact and affordability - the 5th hurdle for cell and gene therapies?
- The European patchwork: EC authorisation is not equal to market access
- EU developments contrasted with the global viewpoint – United States and Asia
- How to assess the value (cost-effectiveness) of potential "one and done" cures
- Next-Generation market access strategies that integrate patient-centric real-world evidence
- Mitigating payer uncertainty: value demonstration with limited clinical data
- Developing an ATMP value dossier and full-spectrum life-cycle evidence generation strategy, employing the complete toolbox to improve value demonstration targeted to all stakeholders
- Differentiated value communication to stakeholders: involving patients and improving education to prepare the community and facilitate access to ATMPs
- ATMP value assessment trends - holistic approaches: Mechanism of Coordinated Access (MoCA), ORPH-VAL, the new AIFA Innovation Algorithm, Impact HTA
- Innovative contracting proposals and Managed Entry Agreements (MEAs) for high-cost gene and cell therapies – theory and practice
- Logistical challenges of a living therapeutic: determining treatment centers and GMP facilities
- Thoughts on business planning: the key success factors for ATMP start-ups and portfolio strategy: ecosystem, tractability, speed, de-risking, funding, valuation, exit strategy

Key Takeaways, Final Q&A and Wrap Up

Interactive Case Studies:

- Kymriah: US pricing expectations of healthcare stakeholders vs analysts and investors; indication-based pricing vs Yescarta; HTA assessments and performance-based contracts in Europe
- Luxturna (adeno-associated viral vector - AAV - gene therapy) pricing and market access success and challenges: US vs NICE England, HAS France, GBA Germany
- Spinal Muscular Atrophy (SMA): Zolgensma (in vivo gene therapy) vs Spinraza (RNA oligonucleotide therapy) market access and payer negotiations
- NICE's Highly Specialised Technology (HST) appraisal of Strimvelis in an ultra-rare population (ADA- SCID)
- AIFA Italy's Performance-Based Risk-Sharing Arrangements and monitoring registries

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