Biannual newsletter **March 2025**

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DARE-NL Annual Consortium Meeting 2025

The DARE-NL Annual Consortium Meeting will once again bring together a diverse and engaged community of ATMP researchers, clinicians, regulators, industry leaders, and policymakers to discuss the latest advancements and challenges in the field. As ATMP development continues to evolve, navigating regulatory frameworks and forging strong partnerships are more crucial than ever to ensure these innovative therapies reach patients faster. This year's meeting will focus on two critical enablers of ATMP implementation: navigating regulatory frameworks and building strategic collaborations.

We are excited to welcome an outstanding lineup of speakers, including Gwylim Janssens, PharmD, who will unravel the gray area of hospital exemption in The Netherlands and Prof. Dr. Christian Chabannon, who will provide insights into the hospital exemption framework from an end-user perspective. Prof. Dr. Ir. Wim Goettsch and Riam Al Dulaimi, PharmD will explore the impact of the start of EU Health Technology Assessment regulations.
Dr. Friso Smit will highlight key initiatives that help bridge the gap from development to clinical practice, after which Hans Schikan, PharmD, will share his perspectives on partnerships, innovation, and accelerating patient access.
The last session starts with a dedicated break-out session where participants can engage in small-group discussions with key opinion leaders on challenges and solutions in ATMP manufacturing. We are pleased to announce that Prof. Dr. Ulrike Köhl will deliver the keynote lecture on ATMP manufacturing strategies.

Beyond the speaker sessions, the meeting will be an excellent opportunity to reconnect with colleagues, explore sponsor demonstrations, and discuss how we can work together to overcome barriers to ATMP adoption.

Whether you are involved in research, clinical application, policy, or manufacturing, this is your opportunity to be part of a dynamic and solution-driven discussion shaping the future of ATMPs. So do not miss out on this unique opportunity to meet and discuss current ATMP developments with a diverse array of experts and register here. Already 65 people have registered and we can host 150 this year, so make sure you secure your (free) ticket on time.
We look forward to welcoming you at the Princess Máxima Center on 19 September!

DARE-NL PROJECT HIGHLIGHTS

WP1: Setup of DARE-NL data, training and valorization platform

Lead: Emma de Pater, Erasmus Medical Center

The ATMP education platform has been extended

The Courses tool has been revamped, so in addition to a broad repository of courses, you can now also find upcoming and previous events (with recordings) and navigate to directories that host a variety of ATMP-related courses. Based on the questions received we gather that the tool is actively being used. Continue to make this tool valuable for ATMP professionals by listing more courses and events and leaving reviews about courses you attended. Contact me for a banner (picture above) to link to the tool on your (institute's) website.

Eighty ATMP professionals came together at the UMC Utrecht on 24 March to attend a **workshop for and by DARE-NL ATMP operators**. Experiences were shared in plenary presentations and insights discussed in break-out groups by operators from across the DARE-NL partner institutes. All operators work apply similar procedures developing ATMPs at the different sites, but this was the first time for them to all get together, get to know each other and find out who does what how and why. It turns out that everybody performs similar procedures just a little bit differently, and there is a lot we can share in DARE-NL to help each other! The ways suggested to do this will be followed up on soon and a summary of key take aways will be shared with attendees and on the DARE-NL SharePoint. There was a lot of enthusiasm for this workshop to be repeated next year! Find the program and pictures online.

A business plan for a sustainable DARE-NL infrastructure is in development

The draft **sustainability model** has been discussed further with the steering committee, scientific and patient advisory boards, Oncode Institute, the IP management committee and KWF. All input is worked out and further input is gathered from several external parties.
Oncode Institute is working on an informal **FTO analysis** around CRISPR-Cas.

After two years **Susette Lauwen** is leaving the UMCU and DARE-NL. We would like to thank Susette for her work in setting up and maintaining our IT infrastructure, including the website, Teams/SharePoint and Zenya, and working on the quality system. Susette supported the setup of the courses tool as well as batch record digitalization efforts and was always ready to lend a hand or step in wherever needed. Her dedication, flexibility, and willingness to support the team will be greatly missed. We wish her all the best in her next endeavors!
For the time being, you can direct questions about Teams or Zenya to info@dare-nl.nl or directly to b.s.punt-2@umcutrecht.nl.

WP2: Harmonizing GMP processes for the manufacturing of cancer-specific ATMPs

Lead: Trudy Straetemans, University Medical Center Utrecht

Inventory of approved materials and specifications complete (WP2.1)

The **overviews of raw materials and suppliers**, as well as the procedure for raw material risk assessment, are available in the Zenya QMS. This marks the completion of milestone 2.1.

Centralized audits performed with harmonized documentation (WP2.2)

The procedure for the **qualification of suppliers** has been published Zenya. Suppliers used by more than two centers are audited, marking the completion of milestone 2.2.

Harmonization of GMP procedures (WP2.3)

Harmonized procedures are established and harmonized across the DARE-NL centers. The first procedure "Harmonized practical guidance: assessment on

excursions of environmental monitoring" has been published in Zenya. This has started its implementation phase – an implementation strategy has been provided to DARE-NL members.

The second practical guidance on the 'aseptic process validation' is almost ready to be sent to all centers and the kick-off for the third procedure on the 'validation of closed automated culture systems' is scheduled on 25 March, already having initiated the sharing of documentation.

The **sharing of structured inspection results** is an ongoing process.

Manufacturing procedures and digital batch record systems (WP2.4)
The survey on ATMP facilities organization and manufacturing procedures setup together with GoCART, T2Evolve, EBMT and NXTGEN-HIGHTECH is under analysis by DARE-NL and NXTGEN-HIGHTECH. The first data will be presented by Trudy Straetemans and Zsolt Sebestyén at the EBMT annual meeting in Florence in March/April.
Characteristics of available **digital batch record systems** are inventoried and compared. Based on this, three providers will provide a demonstration.

WP3: QC harmonization and assay development

Lead: Inge Jedema, NKI/AVL

Development and implementation of QC assays is ongoing (WP3.1/3.2)
The template to validate **cell counting** methods according to the new EP2.7.29 guideline was drafted and discussed over summer. After optimizing the validation protocol, the round robin test for manual cell counting was performed in January/February. Results are under analysis and will be shared and discussed.

Inventory of QC requirements in the EU, USA, and UK is ongoing (WP3.3)
Different ATMP products in development by DARE-NL partners are undergoing a marketing authorization application (MAA) procedure or are the topic of exploratory advice meetings with the CBG/EMA. **Interaction with the EMA** on specific QC assays for these products has started as part of the ongoing procedures and lessons learned are shared within DARE-NL.

WP4: Setup of a Dutch academic GMP vector manufacturing platform

Lead: Edwin Bremer, University Medical Center Groningen

GMP-ready lentiviral production platform is under development (WP4.1)
The first **GMP-grade lentivirus batch** is planned to be delivered by the end of this year. Downstream processing steps for purification and formulation have been defined and are being developed for tech transfer. The **pDARE-NL vector** has been distributed and is in use in multiple academic centers.

Successful establishment of GMP-ready retroviral production platform (WP4.2)
Retroviral vectors have been produced in **scalable cell culture vessels**. Downstream processing steps for retroviral pre-treatment, filtration and concentration have been defined.

Establishment of process controls is under development (WP4.3)
Quality controls for lentiviral production have been established, with one final control currently under validation.

WP5: Identification and implementation of new technologies for the development and GMP-compliant manufacturing of ATMPs

Lead: Harry Dolstra, Radboud University Medical Center

Roadmap for new technologies implementation is under development (WP5.1)
The second **WP5 symposium** was organized on 26 November at the UU. Each center presented their needs in terms of reagents and devices in the context of WP5 for the coming years, as well as what they would be able to contribute. Cell & Gene Therapy CDMO Aldevron presented their GMP-grade products and services around DNA, RNA and enzymes in the afternoon. We finished the day with a plenary discussion on how to move forward with WP5, focusing on the following topics:

- The roadmap/publication on current guidelines for the clinical translation of CRISPR-based gene-edited cell products
- Production of GMP-grade buffers and RNA
- Obtaining a European subsidy
- Collaboration with a small biotech company

A very interactive discussion led to many decisions and new action items.

Route for manufacturing GMP-grade CRISPR-Cas is designed (WP5.2/5.3)
We are exploring different possibilities when it comes to obtaining **GMP-grade CRISPR reagents**, ranging from in-house production in one academic center

to production in a dedicated pharmacy to joint outsourcing of the production with a company willing to lower its prices to a level that would be affordable for the Dutch academic centers. An additional option under consideration is to apply for a grant with European collaborators.

WP6: Regulation, health economics, health technology assessment and patient access

Lead: Pauline Meij, Leiden University Medical Center

Overview of manufacturing, evidence, HTA and regulatory pathways (WP6.1)
A workshop focused on **regulatory affairs** was held on 17 October. In this first edition the focus was on the (Quality) Target Product Profile, the Pediatric Investigational Plan, Platform Technologies, and exploring how the knowledge from the Market Approval Course can be used to improve product development, as demonstrated by the case of CAR-NK cell therapy development. We thank all DARE-NL participants who presented, and the regulatory affairs specialist Ineke Jonker-Hoogerkamp for her guidance during the preparations and for the insightful discussions during the workshop. We also thank everyone who attended and hope to receive everyone again on a next edition, where other topics will be explored – stay tuned for more information.
The HTA roadmap was also presented and discussed during and is now being finalized for publication. Another presentation was provided by FarmInform, a data trust collecting data on the use of pharmaceutics from various stakeholders. The LUMC initiated a collaborative aimed to evaluate the suitability of this platform to share data on ATMP use through the Hospital Exemption pathway.

The framework for the **regulatory roadmap** has been established. With the help of a web developer, we are currently exploring the possibility of hosting the roadmap as an interactive tool on the DARE-NL website.

Tool to assess academic CGT-specific development costs (WP6.2)
The design and pilot of the **CGT costing tool** has been finalized. Implementation is a work in progress. Two teams from the Radboudumc and LUMC are eager to start using the costing tool, which is planned for this year.

The TCR-T therapy product developed at the LUMC, also by Mara Tihaya in the DARE-NL Regulatory Affairs program, has been selected as a case to be presented at the fifth listen-and-learn focus group meeting of the EMA Quality Innovation Group in April.

Stakeholder sandbox topic: ATMP-NL (WP6.3)
A DARE-NL workshop was organized on **Regulatory Sciences, HTA and ATMP-NL** at the LUMC on 25 March. Christine van Hattem, PhD candidate Regulatory Sciences in DARE-NL at the UU, shared progress on the studies she works on for her thesis titled ‘Promises and challenges across the lifecycle of cell and gene therapies’. Jurriaan Gort, DARE-NL PhD candidate at the UMC Utrecht, provided an update on his work in Health Technology Assessment with an overview of the landscape analysis, challenges, roadmap, root cause analysis, costing tool and business plan.
The RSNN SIG Advanced Therapies sandbox developed in DARE-NL WP6 has been instrumental in developing the groundwork for ATMP-NL. RSNN SIG co-chair Lourens Bloem presented the bottlenecks for patient access to ATMPs identified in the RSNN 2023 multistakeholder workshop and the resulting ZonMw-financed report 'Geneesmiddelen voor Geavanceerde Therapie (ATMPs) in Nederland: Veldverkenning, Knelpuntenanalyse en Activiteitenkaart’, written by Jurriaan, Christine, Lourens and Renske. The need for a national ATMP network was further explored in the RSNN/FAST 2024 workshop, with the report titled 'Shaping the potential of ATMP-NL' published in January. These reports concluded a clear need for a national ATMP network to facilitate sustainable patient access to ATMPs by addressing fragmentation of the Dutch ATMP field.
Special guest Mike Broeders (FAST) then shared the FAST approach to facilitate the shaping of ATMP-NL, with the goal to connect existing initiatives and foster collaboration, followed by a plenary discussion on the goals, responsibilities, ensuring of stakeholder alignment and long-term sustainability. FAST will further work out the ATMP-NL initiative, aiming to launch the platform later this year.

The workshop was followed by the biannual ATMP working party meeting. Minutes will follow shortly.

For 2025-2026, at least three more RSNN SIG ATMP workshops/expert meetings are planned on topics relevant/closely related to the interests and activities of DARE-NL, including one about novel business models.

An HE and trial registry for ATMPs are in development (WP6.4)
The CCMO is finalizing the **new trial registry**. The previous version of the registry was known as the ‘Landelijk Trial Register (LTR)’. The current registry is called ‘Overzicht van Medisch-wetenschappelijk Onderzoek in Nederland (OMON)’. DARE-NL is liaising with the CCMO to make trials with ATMPs visible and searchable in this registry. We have been planning a trial registry symposium, together with the CCMO and IKNL, to showcase the new trial registry and expect to host this event in Q4 of 2025.

The latest news on the HE registry in the Netherlands was presented in a European Committee meeting focused on the implementation of the Hospital Exemption in the EU and attended by ATMP developers, regulators, national competent authorities and the pharmaceutical industry in November 2024. A registry for The Netherlands will be developed by the CBG/MEB. To bridge the time until this HE registry becomes available and accessible to all stakeholders, we intend to share a list of ongoing HE in the DARE-NL-affiliated research centers in Zenya. All DARE-NL partners will be contacted with a questionnaire about ongoing ATMPs under HE. This information will be shared exclusively with DARE-NL members.

Involvement of a patient advisory board throughout the activities of DARE-NL (WP6.5)
PAB member Violeta Astratinei presented DARE-NL achievements and goals at the MPNEhub2024 on 6 December. Atefeh Sadeghi (Inspire2Live) replaces Nicole Plum in the Patient Participation Review Committee. Atefeh’s drive is to promote collaboration, nicely aligning with the ambition of DARE-NL. Welcome Atefeh and thank you for your efforts to improve patient engagement!

PUBLICATION HIGHLIGHTS IN THE FIELD OF ATMPS

The three main cancer charities and the cabinet of the Minister of Health in Belgium have requested the Belgian Health Care Knowledge Centre KCE to prepare a roadmap for the development of academic cell therapies in Belgium, with a focus on legal aspects. Before implementing a concrete roadmap, they published a report on the roadmap 'pre-conditions', exploring the legal and organizational strategy for the academic development of ATMPs in Belgium (KCE, Jan 2025).

A multistakeholder workshop was organized by RSNN-SIG ATMPs and FAST with the aim to investigate The need for a national ATMP network. The report summarizes the workshop's discussions, concluding a clear need for a national ATMP network in NL (RSNN, Dec 2024).

FAST collaborated with experts to create a renewed and expanded guidebook for developing ATMPs in the Netherlands. Tailored to both academic and commercial developers, the guidebook delivers essential guidance on European and Dutch regulations and provides a roadmap to navigate the complex ATMP development process (FAST, Nov 2024).

The Dutch Ministry of Health, Welfare and Sport asked FAST to draw an overview of bottlenecks, solutions, and stimulatory measures in academia-driven drug development, executed by consulting firm SiRM (in Dutch, FAST, Oct 2024).

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 February 2025
EMA/CAT/52354/2025
Human Medicines Division

CAT quarterly highlights and approved ATMPs
February 2025

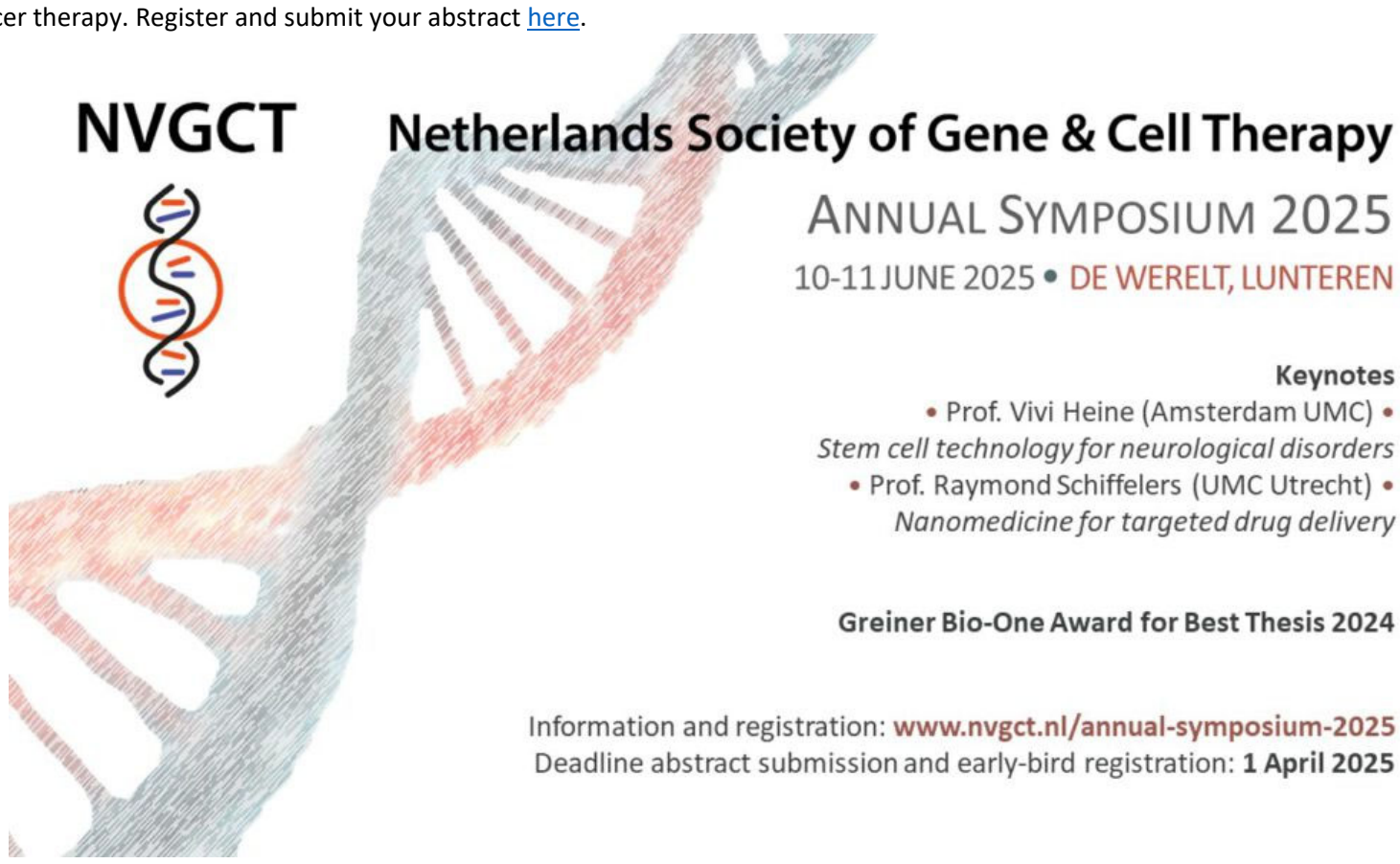
Quarterly highlights and approved ATMPs by the Committee for Advanced Therapies

ATMP LANDSCAPE: WHAT HAPPENS IN THE NETWORK

FAST published the ATMP guidebook, which many DARE-NL representatives contributed to.

An amendment regarding the Safety and Quality of Body Material Act was submitted earlier this month, with the aim to prohibit making a profit on products that use bodily cells or tissue as raw material. Swift reponses by NVvH, HOVON (IEC), Hematon and industry led to an adjustment so the amendment now comprises an obligation to monitor the effects of the law on donor safety and willingness to donate in two years.

DARE-NL will host a session at the Netherlands Society of Gene and Cell Therapy (NVGCT) Annual Symposium this year. Trudy Straetemans will introduce DARE-NL and provide a presentation on the clinical development of TEG cells for cancer therapy, Edwin Bremer will provide a presentation on the academic lentiviral vector production platform in the Netherlands and Harry Dolstra will provide a presentation on the clinical development of CAR-NK cells for cancer therapy. Register and submit your abstract here.



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