Scope of this talk

- Increasing interest in academic drug development.
- Regulatory systems are never perfect, they evolve over time, are exposed to push and pull dynamics.
- Regulatory science is there to improve regulatory standards, procedures and decision making, but also to understand how things work, can be improved.
- Two recent show cases of regulatory science may help to increase awarenesss and learning:
  - Drug repurposing for rare diseases
  - Extension of indications of licensed products
- Regulatory Science Network Netherlands aims to add.

Evolution of Regulatory Science in NL

2007-2012

TI Pharma Escher Project

2012-2017

MEB as catalyst for the big jump

2017-2022

RSNN and multistakeholder engagement

Drug Repurposing for Rare Diseases: A Role for Academia

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Background: The European Commission highlights in its Pharmaceutical Strategy the role of academic researchers in drug repurposing, especially in the development of orphan medicinal products (OMPs). This study summarizes the contribution of academia over the last 5 years to registered repurposed OMPs and describes barriers to success, based upon three real world cases.

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- 2016-2020, 68 new orphan drugs in Europe.
- 13/68 the outcome of a repurposing trajectory.
- 75% academic, 25 % industry.
- Academic development primarily new indication, industry more focus on new application.

Regulatory-HTA roadmap

	Critical	Why?
CTD Module 3 (Quality/CMC)	++	Few 'simple' oral formulations, but also PEG/-liposomals, nebuliser, complex gels, eyedrops
CTD Module 4 (Non-clinical)	+/-	13/13 APIs known for >20 year, ample safety data, 10/13 with >5,000 PubMed publications
CTD Module 5 (Clinical)	+++	Small numbers, heterogeneity of patients, study design, outcome/estimand, completion trials, B/R
ICH E2D Post-approval safety data	++	ADR reporting, registries, post-approval data, off-label, pregnancy exposure, risk minimisation, RWD
HTA, access, pricing, reimbursement	+++	Bumpy HTA trajectories, 4/13 erratic pricing, pharmacy compounding as alternative, limited access

Extension of Indication for Authorised Oncology Products in the European Union: A Joint Effort of Multiple Stakeholders

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After marketing authorisation, the development of a medicinal product often continues with studies investigating new therapeutic indications. Positive results can potentially lead to changes to the terms of the marketing authorisation, such as an extension of therapeutic indication(s). These studies can be initiated and sponsored by the marketing authorisation holder (MAH) or by others. When results from an investigator-initiated

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8: 790782.

- Investigator-initiated trials are an important (additional) source for building clinical evidence.
- New evidence can justify regulatory extension of indication in the product label.
- There are mixed incentives for stakeholders i.e. investigator, MAH, prescribers to follow that route.

Regulatory-HTA roadmap

	Critical	Why?
CTD Module 3 (Quality/CMC)	+/-	Product is already on the market
CTD Module 4 (Non-clinical)	+/-	Product is already on the market
CTD Module 5 (Clinical)	+++	Are new indications left-overs or missed oppor-tunities? study design, outcome/estimand, B/R
ICH E2D Post-approval safety data	++	New indication > new exposures > may require registries, extra and targeted post-approval data
HTA, access, pricing, reimbursement	+++	Who wins, who loses, willingness to pay, what if MAH does not want to extend the label?

What can we learn and future outlook

- Regulatory science provides a window of opportunities for learning for academic drug developers.
- There are exceptions, but overall academia has not a strong record of bringing promising medicinal products from bench to license.
- RSNN and partners will develop and implement three layer model of regulatory dialogue and guidance > [1] Help desk, [2] Tailoring most suitable regulatory pathway(s), [3] Thinktanking.
- Conceptual framework: Technology Readiness Levels.
- Critical success factors: governance of responsibilities, interests and liabilities, avoiding regulatory capture, international alignment.