
Scanning your horizon
•Detect promising products early!
tips & tricks for Community Advisory Boards

“

“Horizon scanning systems aim to identify, filter, and prioritise new and emerging health technologies; to assess or predict their impact on health, costs, society, and the health care system; and to inform decision makers and research planners.”

• — EUROSCAN 2014

In this presentation

Horizon scanning

Advice

Please share this training with your peers. Horizon can best be scanned when different people look in all directions!

Scan your horizon
What do you need it for?

Identify
Technologies of interest to you

Organise
the information and prioritise

Examples

What would you scan your horizon for?

And so much more!

•1

- Know which products or projects should be priority: medicines, devices…
- CAB planning

•2

- Be exhaustive when communicating on trials to your members
- no publicity: all, or none

•3

- Plan negotiations: compassionate use programmes, multi-investigational product trials…

•4

- Learn which teams or investigators are active in your field

•5

- Discuss and share results of your scan with regulators and HTA doers

•FACTS
•EU register of pharmaceuticals

Disease	Number of designated orphan products
Cystic Fibrosis	24
Systemic Sclerosis	12
Hepatocellular carcinoma	15
Glioma(s)	24
Lymphoma(s)	37
Niemann-Pick	5
Beta-Thalassemia	5
Myastenia Gravis	3
Multiple Myeloma	7

For your own disease, do you know how many products are in R&D phase?

Ask yourself

- And also: medicines only, or other technologies? In vitro diagnostics? Implantable devices? Connected devices?

• Which time horizon? How far in the pipeline?

From pre-clinical stage? From proof of concept studies? From confirmatory studies? From their results?

• National agencies do horizon scanning

So doe the EMA or HTA bodies. Consider exchanging views with them.

• For example consult

Early Warning System DACEHTA (Denmark)

Alert System SBU (Sweden)

Emerging Drug List CADTH (Canada)

Horizon Scanning in oncology (Austria)


Your disease
•How do you name it?
OrphaCode

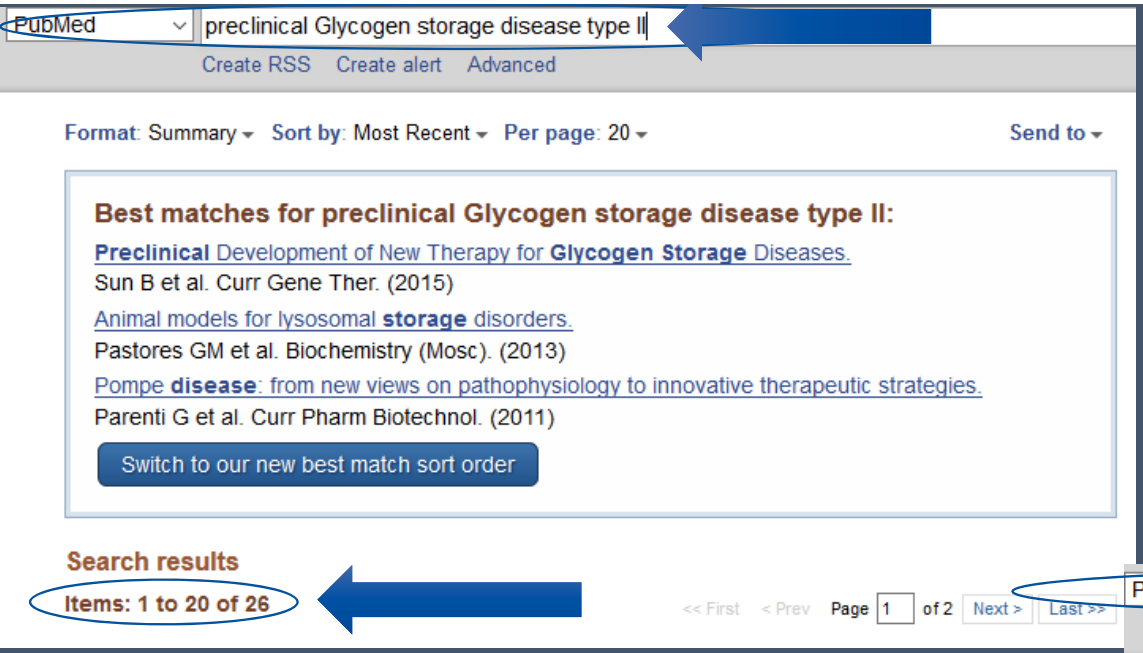
SYNONYMS

Example: Pompe disease (36)

Alpha-1,4-glucosidase acid deficiency
GSD due to acid maltase deficiency
GSD type 2 - GSD type II
Glycogen storage disease type 2 - Glycogen storage disease type II
Glycogenosis due to acid maltase deficiency
Glycogenosis type 2 - Glycogenosis type II (28)

Age of onset:
Antenatal, Neonatal
Infancy, Childhood
Adolescent
Adult

ORPHA:365
ICD-10: E74.0
OMIM: 232300
UMLS: C0017921
MeSH: D006009
GARD: 5714
MedDRA: 10053185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Preclinical Development of New Therapy for Glycogen Storage Diseases.
Sun B et al. Curr Gene Ther. (2015)
Animal models for lysosomal storage disorders.
Pastores GM et al. Biochemistry (Mosc). (2013)
Pompe disease: from new views on pathophysiology to innovative therapeutic strategies.
Parenti G et al. Curr Pharm Biotechnol. (2011)
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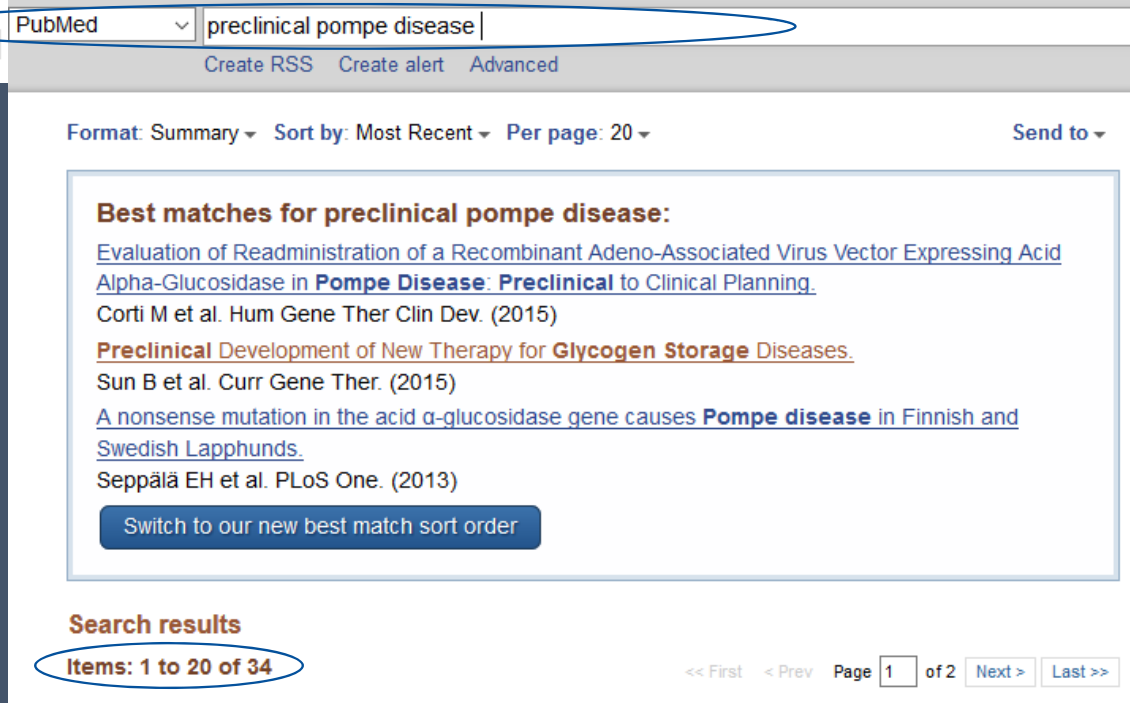
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Evaluation of Readministration of a Recombinant Adeno-Associated Virus Vector Expressing Acid Alpha-Glucosidase in Pompe Disease: Preclinical to Clinical Planning.
Corti M et al. Hum Gene Ther Clin Dev. (2015)
Preclinical Development of New Therapy for Glycogen Storage Diseases.
Sun B et al. Curr Gene Ther. (2015)
A nonsense mutation in the acid α-glucosidase gene causes Pompe disease in Finnish and Swedish Lapphunds.
Seppälä EH et al. PLoS One. (2013)
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Pre-clinical stage

- Academic research

Proof-of-concept

- Early trials in humans – products that could work

Confirmatory trials

- Products that seem to be effective

•1 identify

- Your main source: Pubmed

https://www.ncbi.nlm.nih.gov/pubmed

PubMed comprises more than 28 million citations for biomedical literature from MEDLINE, life science journals, and online books

- **Citations may include links to full-text content from PubMed Central and publisher web sites**

No need to go beyond 10-15 years | SPEED

Focus on recent scientific work

•Identify 1

- You may find topics you didn't think of in the first place

☐ 3. Treatment with enzyme replacement therapy during pregnancy in a patient with **Pompe** disease.
Holbeck-Brendel M, Poulsen BK.
Neuromuscul Disord. 2017 Oct;27(10):956-958. doi: 10.1016/j.nmd.2017.06.556. Epub 2017 Jul 5.
PMID: 28735900
Similar articles

Be curious

- Share the work with your peers
- **Record the information you find, someone might use it later**

Molecular Therapy
Original Article

AMERICAN SOCIETY of GENE & CELL THERAPY

Duvoglustat HCl Increases Systemic and Tissue Exposure of Active Acid α-Glucosidase in Pompe Patients Co-administered with Alglucosidase α

Priya Kishnani,[1] Mark Tarnopolsky,[2] Mark Roberts,[3] Kumarswamy Sivakumar,[4] Majed Dasouki,[5] Mazen M. Dimachkie,[5] Erika Finanger,[6] Ozlem Goker-Alpan,[7] Karl A. Guter,[8] Tahseen Mozaffar,[9] Muhammad Ali Pervaiz,[10,20] Pascal Laforet,[11] Todd Levine,[12] Matthews Adera,[13] Richard Lazauskas,[14] Sheela Sitaraman,[14] Richie Khanna,[14] Elfrida Benjamin,[14] Jessie Feng,[14] John J. Flanagan,[15] Jay Barth,[14] Carrolee Barlow,[16] David J. Lockhart,[17] Kenneth J. Valenzano,[14] Pol Boudes,[18] Franklin K. Johnson,[14] and Barry Byrne[19]

[1]Duke University Medical Center, Durham, NC 27710, USA; [2]McMaster University Medical Center, Hamilton, ON L8N 3Z5, Canada; [3]Salford Royal Hope NHS Trust Hope Hospital, Salford M6 8HD, UK; [4]Neuromuscular Research Center, Scottsdale, AZ 85028, USA; [5]University of Kansas Medical Center, Kansas City, KS 66160, USA; [6]Oregon Health and Science University, Portland, OR 97239, USA; [7]LSD Research and Treatment Unit, O&O Alpan, LLC, Fairfax, VA 22030, USA; [8]Great Falls Clinic, Great Falls, MT 59405, USA; [9]University of California, Irvine, Irvine, CA 92697, USA; [10]Emory University, Decatur, GA 30030, USA; [11]Hopital la Salpetriere Institut de Myologie, 75013 Paris, France; [12]Phoenix Neurological Associates, Phoenix, AZ 85018, USA; [13]Insys Therapeutics, Chandler, AZ 85224, USA; [14]Amicus Therapeutics, Cranbury, NJ 08512, USA; [15]Arvinas, Inc., New Haven, CT 06511, USA; [16]The Parkinson's Institute and Clinical Center, Sunnyvale, CA 94085, USA; [17]TranscripTx, Inc., Sunnyvale, CA 94085, USA; [18]Cymabay Therapeutics, Newark, CA 94560, USA; [19]University of Florida, Gainesville, FL 32611, USA

Duvoglustat HCl (AT2220, 1-deoxynojirimycin) is an investigational pharmacological chaperone for the treatment of acid α-glucosidase (GAA) deficiency, which leads to the lysosomal storage disorder Pompe disease, which is characterized by progressive accumulation of lysosomal glycogen primarily in heart and skeletal muscles. The current standard of care is enzyme replacement therapy with recombinant human GAA (alglucosidase alfa [AA], Genzyme). Based on preclinical data, oral co-administration of duvoglustat HCl with AA increases exposure of active levels in plasma and skeletal muscles, leading to greater substrate reduction in muscle. This phase 2a study consisted of an open-label, fixed-treatment sequence that evaluated the effect of single oral doses of 50 mg, 100 mg, 250 mg, or 600 mg duvoglustat HCl on the pharmacokinetics and tissue levels of intravenously infused AA (20 mg/kg) in Pompe patients. AA alone resulted in increases in total GAA activity and protein in plasma compared to baseline. Following co-administration with duvoglustat HCl, total GAA activity and protein in plasma were further increased 1.2- to 2.8-fold compared to AA alone in all 25 Pompe patients; importantly, muscle GAA activity was increased for all co-administration treatments from day 3 biopsy specimens. No duvoglustat-related adverse events or drug-related tolerability issues were identified.

INTRODUCTION

Pompe disease, also referred to as glycogen storage disorder type II or acid maltase deficiency, is a lysosomal storage disorder (LSD) caused by mutations in the *GAA* gene that encodes the lysosomal hydrolase acid α-glucosidase (GAA).[1,2] Deficiency of GAA activity results in progressive accumulation and deposition of glycogen in the lysosomes of heart, skeletal muscles, and other tissues. The disease encompasses a broad spectrum of phenotypes that range from severe classic infantile Pompe disease to the more slowly progressing late-onset form.[3–5] Late-onset Pompe disease (LOPD) can present as early as the first year of life to adulthood, has a slower rate of progression than the infantile-onset form, and is typically characterized by musculoskeletal and pulmonary involvement that leads to progressive weakness and respiratory insufficiency.[1,3–5] Cardiac involvement can occur in LOPD as well.[4]

Enzyme replacement therapy (ERT) is currently the primary treatment for Pompe disease.[6] ERT is based on the intravenous administration of recombinant human GAA (rhGAA), of which Myozyme and Lumizyme (alglucosidase alfa [AA]; Genzyme) are the only two approved products. Although infantile and late-onset Pompe patients have shown some improvements and stabilization in motor and respiratory functions following therapy with ERT, residual disease persists, suggesting that ERT is not completely effective in clearing glycogen and correcting all of the associated underlying pathologies.[7,8] Despite the clinical benefits of ERT, correction of the skeletal muscle phenotype is particularly challenging, and not all patients

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http://dx.doi.org/10.1016/j.ymthe.2017.02.017.

[20]Present address: WellStar Health Systems, Marietta, GA 30066, USA

Correspondence: Franklin K. Johnson, Amicus Therapeutics, 1 Cedar Brook Drive, Cranbury, NJ 08512, USA.
E-mail: fjohnson@amicusrx.com

•Identify 1

•Lucky

4. Induced pluripotent stem cell models of lysosomal storage disorders.
Borger DK, McMahon B, Roshan Lal T, Serra-Vinardell J, Aflaki E, Sidransky E.
Dis Model Mech. 2017 Jun 1;10(6):691-704. doi: 10.1242/dmm.029009. Review.
PMID: 28592657 Free PMC Article
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5. Duvoglustat HCl Increases Systemic and Tissue Exposure of Active Acid α-Glucosidase in **Pompe** Patients Co-administered with Alglucosidase α.
Kishnani P, Tarnopolsky M, Roberts M, Sivakumar K, Dasouki M, Dimachkie MM, Finanger E, Goker-Alpan O, Guter KA, Mozaffar T, Pervaiz MA, Laforet P, Levine T, Adera M, Lazauskas R, Sitaraman S, Khanna R, Benjamin E, Feng J, Flanagan JJ, Barth J, Barlow C, Lockhart DJ, Valenzano KJ, Boudes P, Johnson FK, Byrne B.
Mol Ther. 2017 May 3;25(5):1199-1208. doi: 10.1016/j.ymthe.2017.02.017. Epub 2017 Mar 22.
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• References 4 and 5: 2 different products

Mol Ther. 2017 May 3;25(5):1199-1208. doi: 10.1016/j.ymthe.2017.02.017. Epub 2017 Mar 22.

Duvoglustat HCl Increases Systemic and Tissue Exposure of Active Acid α-Glucosidase in Pompe Patients Co-administered with Alglucosidase α.

Kishnani P[1], Tarnopolsky M[2], Roberts M[3], Sivakumar K[4], Dasouki M[5], Dimachkie MM[5], Finanger E[6], Goker-Alpan O[7], Guter KA[8], Mozaffar T[9], Pervaiz MA[10], Laforet P[11], Levine T[12], Adera M[13], Lazauskas R[14], Sitaraman S[14], Khanna R[14], Benjamin E[14], Feng J[14], Flanagan JJ[15], Barth J[14], Barlow C[16], Lockhart DJ[17], Valenzano KJ[14], Boudes P[18], Johnson FK[19], Byrne B[20].

Author information

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KEYWORDS: Pompe disease; enzyme replacement therapy; pharmacokinetics; pharmacological chaperone

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Increases Systemic and Tissue Exposure (

25(5):1199-1208. doi: 10.1016/j.ymthe.2017.02.017. Epub 2017 Mar 22.

Duvoglustat HCl

HCl Increases Systemic and Tissue Exposure of Active Acid α-Glucosidase in Pompe Patients Co-administered with Alglucosidase α.

Kishnani P[1], [illegible]olsky M[2], Roberts M[3], Sivakumar K[4], Dasouki M[5], Dimachkie MM[5], Finanger E[6], Goker-Alpan O[7], Guter KA[8], Mozaffar T[9], Pervaiz MA[10], Laforet [illegible]era M[13], Lazauskas R[14], Sitaraman S[14], Khanna R[14], Benjamin E[14], Feng J[14], Flanagan JJ[15], Barth J[14], Barlow C[16], Lockhart DJ[17], [illegible] P[18], Johnson FK[19], Byrne B[20].

1 [illegible]enter, Durham, NC 27710, USA.
2 [illegible]al Center, Hamilton, ON L8N 3Z5, Canada.
3 [illegible]rust Hope Hospital, Salford M6 8HD, UK.
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6 [illegible] Science Uni[illegible]d, OR 97239, USA.
7 LSD Research and Treatment Unit, U[illegible] C, Fairfax, VA 22030, USA.
8 Great Falls Clinic, Great Falls, MT 59405, U[illegible]
9 University of California, Irvine, Irvine, CA 92697, US[illegible]
10 Emory University, Decatur, GA 30030, USA.
11 Hopital Ia Salpetriere Institut de Myologie, 75013 Paris, France.
12 Phoenix Neurological Associates, Phoenix, AZ 85018, USA.
13 Insys Therapeutics, Chandler, AZ 85224, USA.

14 Amicus Therapeutics, Cranbury, NJ 08512, USA.

[illegible] The Parkinson's Institute and Clinical Center, Sunnyvale, CA 94085, USA.
17 TranscripTx, Inc., Sunnyvale, CA 94085, USA.
18 Cymabay Therapeutics, Newark, CA 94560, USA.
19 Amicus Therapeutics, Cranbury, NJ 08512, USA. Electronic address: fjohnson@amicusrx.com.
20 University of Florida, Gainesville, FL 32611, USA.

. Electronic address: fjohnson@amicusrx.com.

Start organising the information

•1

- Product name (active substance, code)

•2

- Activity (enhancer, acting on the cause, symptomatic…)

•3

- Academic teams in Europe

•4

- Developer name, contact details

•5

- Download free article

•1

•Read the abstract

Extract more information

- Pre-clinical? Phase 1? 2? 2a? 2b? 2-3? 3?
  - **Be selective**

Author information

Abstract

Duvoglustat HCl (AT2220, 1-deoxynojirimycin) is an investigational pharmacological chaperone for the treatment of acid α-glucosidase (GAA) deficiency, which leads to the lysosomal [illegible] progressive accumulation of lysosomal glycogen primarily in heart and skeletal m[illegible]ent t[illegible] human GAA (alglucosidase alfa [AA], Gen[illegible] levels in plasma and skeletal [illegible]sure of active fixed-treatment sequence that evaluated the effect of single oral doses of 50 mg, 100 mg, 250 mg, or 600 mg duvoglustat HCl on the pharmacokinetics and tissue levels of intravenously infused AA[illegible]dy consisted of an open-label, activity and protein in plasma compared to baseline. Following [illegible]. AA alone resulted in increases in total GAA [illegible]stat HCl, total GAA activity and protein in plasma were further increased 1.2- to 2.8-fold compared to AA alone in all 25 Pompe patients; importantly, muscle GAA activity was increased for all co-administration treatments from day 3 biopsy specimens. No duvoglustat-related adverse events or drug-related tolerability issues were identified.

oral co-administration of duvoglustat HCl

phase 2a study

50 mg, 100 mg, 250 mg, or 600 mg duvoglustat HCl

25 Pompe patients

KEYWORDS: Pompe disease; enzyme replacement therapy; pharmacokinetics; pharmacological chaperone

Start organising the information

•6

- Administration mode (oral, IV, SubC, topical…)

•7

- Doses and regimen

•8

- Development phase

•9

- Early results: activity

•10

- Early results: toxicity, tolerability

Induced pluripotent stem cell

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Dis Model Mech. 2017 Jun 1;10(6):691-704. doi: 10.1242/dmm.029009.

Induced pluripotent stem cell models of lysosomal storage disorders.

Borger DK[1], McMahon B[1], Roshan Lal T[1], Serra-Vinardell J[1], Aflaki E[1], Sidransky E[2].

Author information

1 Medical Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892, USA.

2 Medical Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892, USA sidranse@mail.nih.gov.

Table 2. Summary of iPSC models of lysosomal storage diseases generated to date

Disease	Implicated gene(s)	Reference	Reprogramming method	Differentiation target(s)	Observations	New therapeutics tested
Pompe disease	*GAA*	Kawagoe et al., 2011	Retrovirus	Skeletal myocytes	Glycogen accumulation	
		Huang et al., 2011	Retrovirus	Cardiomyocytes	Substrate accumulation, altered metabolic flux, and disordered myofibrils	–
		Higuchi et al., 2014	Retrovirus	–	Substrate accumulation in iPSCs	–
		Raval et al., 2015	Lentivirus	Cardiomyocytes	Defective protein glycosylation	–
		Sato et al., 2015	Pre-existing lines	Cardiomyocytes	*GAA* overexpression reduces glycogen storage	Gene therapy
		Sato et al., 2016b	Pre-existing lines	Skeletal myocytes	*TFEB* supplements *GAA* overexpression in normalizing glycogen levels	Gene therapy
		Sato et al., 2016a	Pre-existing lines	Cardiomyocytes	Metabolic dysfunction, oxidative stress	–

Sato Y., Kobayashi H., Higuchi T., Shimada Y., Era T., Kimura S., Eto Y., Ida H. and Ohashi T. (2015). Disease modeling and lentiviral gene transfer in patient-specific induced pluripotent stem cells from late-onset Pompe disease patient. *Mol. Ther. Method. Clin. Dev.* 2, 15023 10.1038/mtm.2015.23 [PMC free article] [PubMed] [Cross Ref]

Sato Y., Kobayashi H., Higuchi T., Shimada Y., Ida H. and Ohashi T. (2016a). Metabolomic profiling of pompe disease-induced pluripotent stem cell-derived cardiomyocytes reveals that oxidative stress is associated with cardiac and skeletal muscle pathology. *Stem Cells Transl. Med* 6, 31-39. 10.5966/sctm.2015-0409 [PMC free article] [PubMed] [Cross Ref]

Sato Y., Kobayashi H., Higuchi T., Shimada Y., Ida H. and Ohashi T. (2016b). TFEB overexpression promotes glycogen clearance of Pompe disease iPSC-derived skeletal muscle. *Mol. Ther. Method. Clin. Dev.* 3, 16054 10.1038/mtm.2016.54 [PMC free article] [PubMed] [Cross Ref]

- First step: your literature review
- You might need to cross-check with other sources

Continue, be systematic, exhaustive

And share the workload: 54 articles reviewed by 6 volunteers = 9 each

•Identify 2

- EMA, NIH, WHO publish information on clinical trials

Clinical trial registries

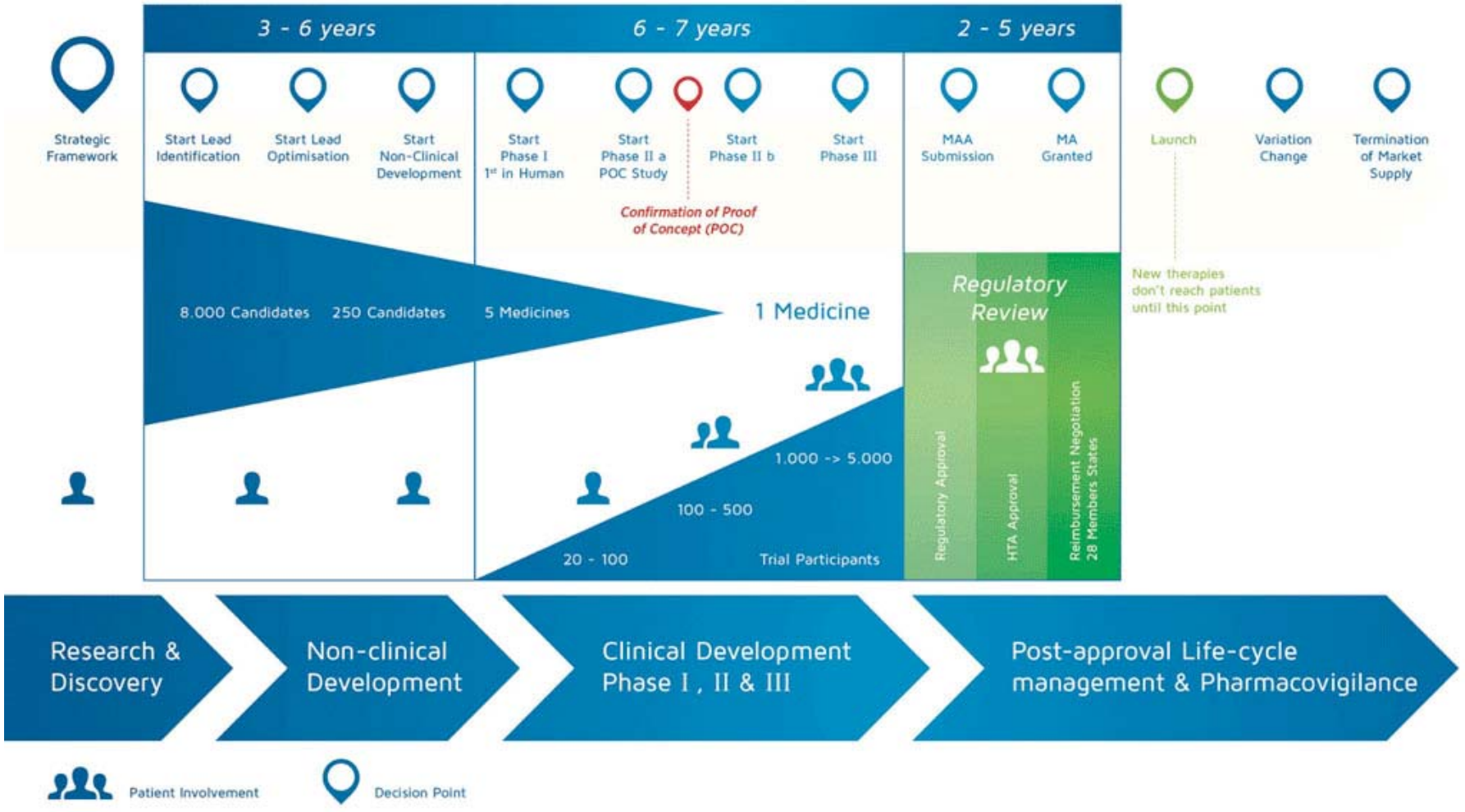
- **Which one to choose?**

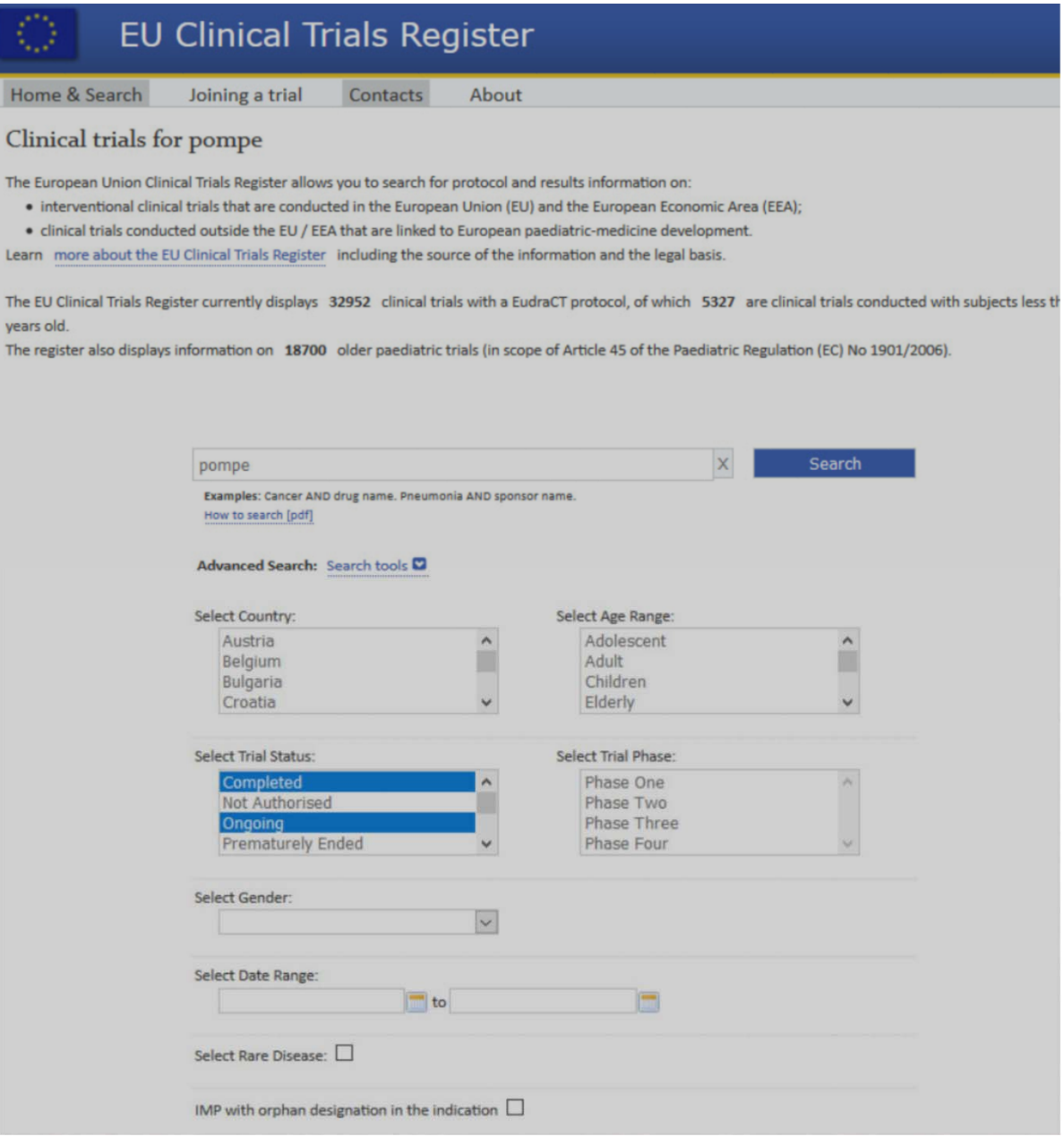
EU Clinical Trials Register

ISRCTN registry

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Overview of Decision Points and Development Steps in Medicines R&D





•2

- The European Register

Use the advanced search

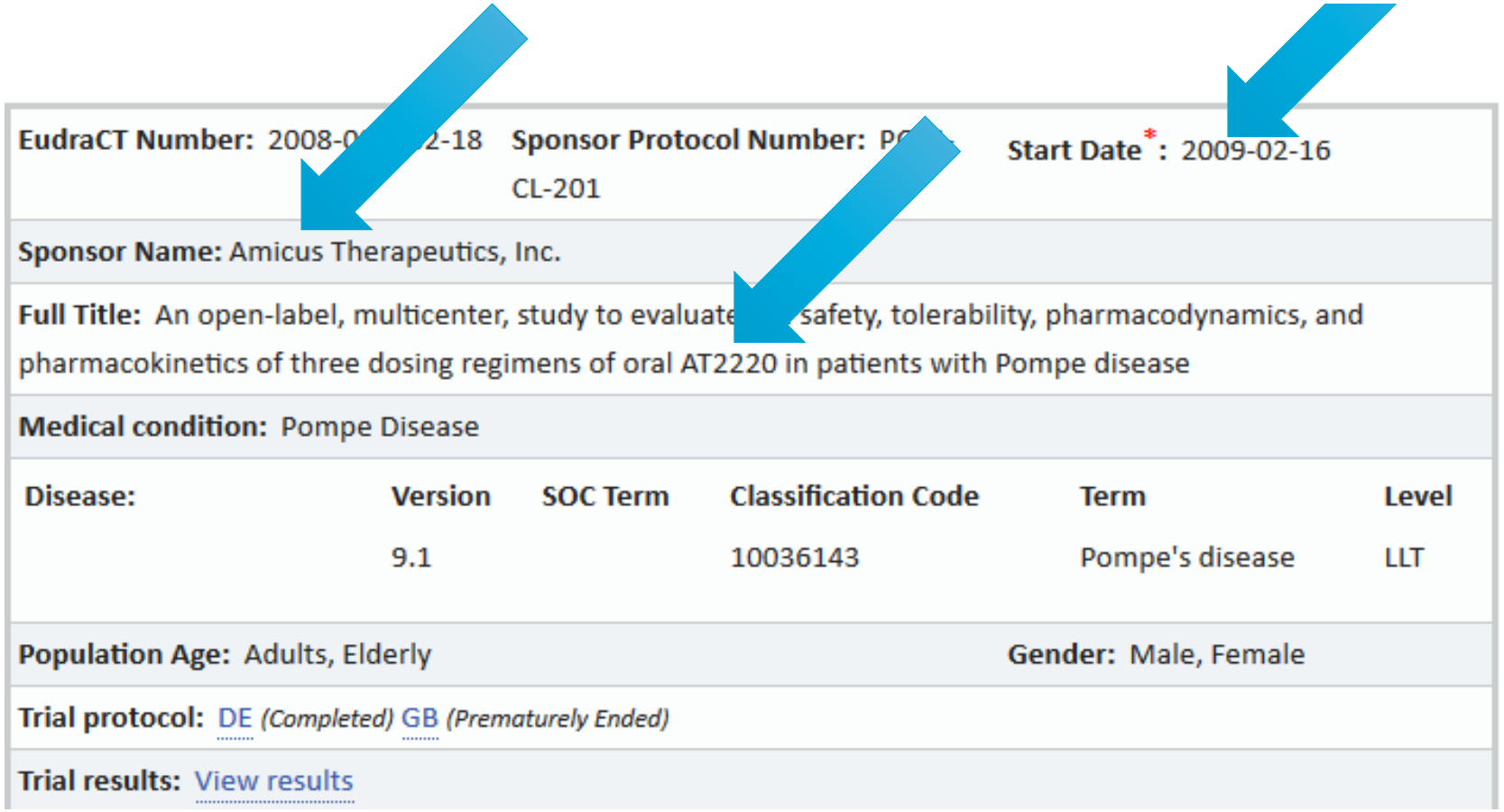
- Who | What | Where | When | Why

•CT search

EU register: 31 completed or ongoing trials |
different creation dates / NIH with early phase 1

NIH: 78 completed or ongoing trials

Will help detect products with clinical trials in humans (phase 1 onwards)



EudraCT Number: 2008-0 -18		**Sponsor Protocol Number:** P CL-201		**Start Date*:** 2009-02-16	
Sponsor Name: Amicus Therapeutics, Inc.					
Full Title: An open-label, multicenter, study to evaluate safety, tolerability, pharmacodynamics, and pharmacokinetics of three dosing regimens of oral AT2220 in patients with Pompe disease					
Medical condition: Pompe Disease					
Disease:	**Version**	**SOC Term**	**Classification Code**	**Term**	**Level**
	9.1		10036143	Pompe's disease	LLT
Population Age: Adults, Elderly				**Gender:** Male, Female	
Trial protocol: DE *(Completed)* GB *(Prematurely Ended)*					
Trial results: View results					

This is the phase 2b trial with duvoglustat, started 2009, published 2017

•Identify 3

- European Register of Pharmaceuticals
  - EMA PRIME scheme
  - FDA Orphan Drug Office

Orphan drug designations

- EU: 6 designated products
- USA: 9 designated products
- Authorised:
  - Myozyme®: EU and USA
  - Lumizyme®: USA

Dr Philippe Moullier 2018

- Adeno-associated viral vector serotype 8 containing the human acid alpha-glucosidase gene

Amicus 2018

- Recombinant human acid alpha-glucosidase

NanoMedSyn 2016

- Recombinant human acid alpha-glucosidase conjugated with mannose-6-phosphate analogues

Genzyme 2014

- Recombinant human alpha-glucosidase conjugated with multiple copies of synthetic bismannose-6-phosphate-tetra-mannose glycan

Audentes therapeutics 2012

- Recombinant adeno-associated viral vector containing human acid alfa-glucosidase-gene

Biomarin 2011

- Glycosylation independent lysosomal targeting tagged recombinant human acid alpha glucosidase

Build a table

Revealing key points enhances comprehension

Class name (e.g. biosimilar, gene therapy…) **Enzyme Replacement**	
Authorised abbreviation **active substance name** *brand name / EPAR* pharmaceutical company	Experimental abbreviation **active substance name** *brand name / SOP* pharmaceutical company
rhGAA **Recombinant human acid alfa-glucosidase** *Myozyme® / EPAR* Genzyme	ATB200 **Rec. hum. alpha-glucosidase with Miglustat** - / *SOP* Amicus therapeutics
Enhancer / Chaperone	
	AT2220 **Duvoglustat** - Amicus therapeutics
Gene therapy	
	- **Adeno-associated viral vector serotype 8 + human acid alpha-glucosidase gene** - Dr Philippe Moullier, 1 rue du Roi Albert, 44000 Nantes, France
	- **Recombinant adeno-associated viral vector + human acid alfa-glucosidase-gene** - / *SOP* Audentes Therapeutics UK Limited

Horizon Scanning for CF

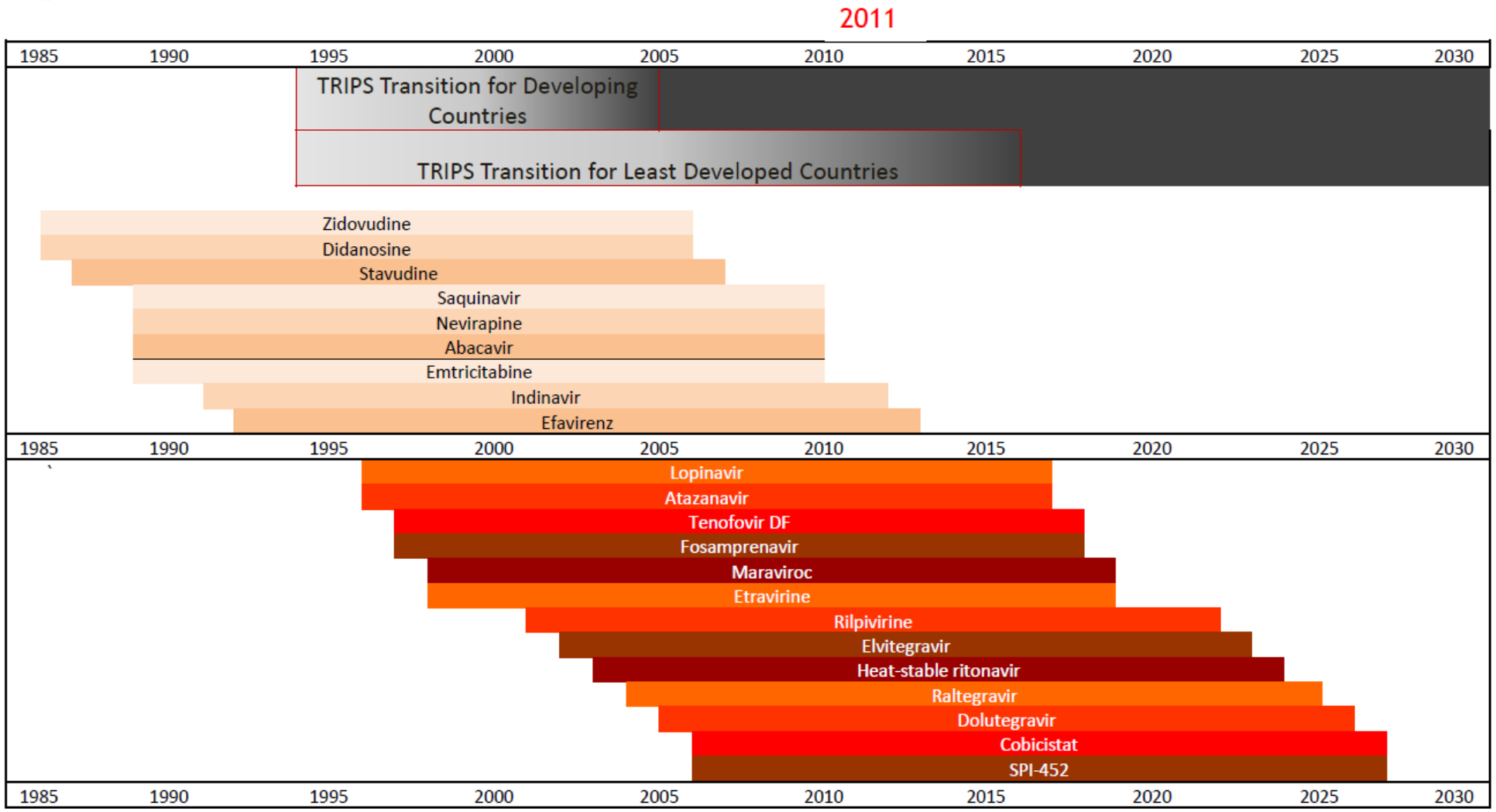
Among recent designations or authorisations:

- 24 products
- 20 companies

Product	Developer	Designation
[redacted]	CURx Pharma (UK) Limited	2015
Multilamellar microvesicle	Lamellar Biomedical Ltd	2011
[redacted]	Mucokinetica Ltd	2010
Nitric oxide	Biological Consulting Europe Ltd	2015
[redacted]	Kither Biotech s.r.l.	2017
Plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene	Imperial Innovations Limited	2014
[redacted]	Plexcera Therapeutics EU Limited	2015
Recombinant human CXCL8 mutant	ProtAffin Biotechnologie AG	2013
[redacted]	Pharm Research Associates (UK)	2011
Sodium nitrite+ethylenediaminetetraacetic acid	Arch Bio Ireland Ltd	2016
Tobramycin (inhalation powder) (TOBI Podhaler)	Novartis Europharm Limited	2003
cyclopentadecane-13,15-dione	Synovo GmbH	2014
[redacted]	Vertex Pharma (Europe)	2014
carboxamide and ivacaftor	Vertex Pharma (Europe)	2017
[redacted]	Clinical Network Services (UK) Ltd	2015
methylpyridin-2-yl)benzoic acid	Vertex Pharma (Europe)	2010
[redacted]	Coté Orphan Consulting UK Limited	2014
4,6,4′–trimethylangelicin	Rare Partners srl Impresa Sociale	2013
[redacted]	TMC Pharma Services Ltd	2016
Alpha-1 proteinase inhibitor	Grifols Deutschland GmbH	2012
[redacted]	PlumeStars s.r.l.	2014
Antisense oligonucleotide	ProQR Therapeutics III BV	2013
[redacted]	NovaBiotics Ltd	2011
oxoquinoline-3-carboxamide (Kalydeco 2012)	Vertex Pharma (Europe)	2008

medicines patent pool

Changing ARV Patent Landscape

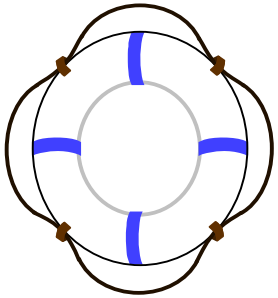


After detecting all products Decide criteria: filter

Agree upon criteria and their respective weights

Collegial

- Gather a group of patients, interview them, discuss limits of available treatment options and what needs to be improved

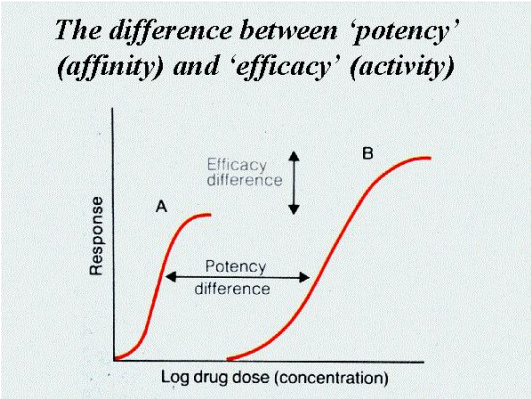


• New mechanism of action

If a first product is authorised and with limited efficacy, a product with a new mechanism of action might be more interesting than a second one of the first class

• In vitro potency

Towards increased efficacy



• Likely to work after failure: rescue treatment

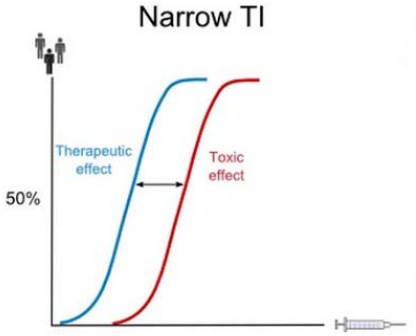
If active for patients who do not respond to standard of care

Collegial

- Gather a group of patients, interview them, discuss limits of available treatment options and what needs to be improved

• Toxicity profile and therapeutic index

Side effects that differ from existing options. If you don't tolerate product A, then maybe you can tolerate the new one



• Interaction with life-style

Food, drinks, diet, sport, herbals, OTC, recreational products…

• Ease of use and constraints

Once a day vs four times a day

24 tablets vs SC injection

Keep at

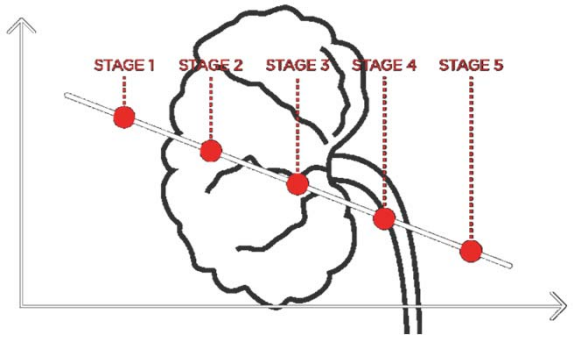
Easy to carry

Collegial

- Gather a group of patients, interview them, discuss limits of available treatment options and what needs to be improved

• Disease stages

Potential to treat all patients, or some only? Are stages clearly defined? Risk for off-label use?



• Patient populations

All to benefit, or contra-indicated for some? E.g. pregnancy, certain age groups…

• And so many others

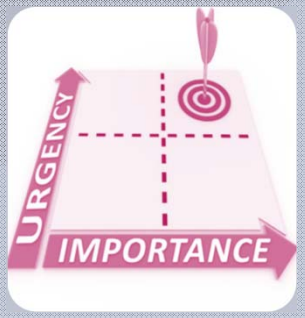
To favour a product likely to be reasonably costly (e.g. second medical use), or easy to manufacture with reduced risk of shortage/defect…

•Working relations

Sponsor supports the OMP policy (orphan designation)

Sponsor requested or plans to request EMA scientific advice or protocol assistance

Sponsor requested or plans to request Early Dialogue (HTA) or parallel SA or MOCA



Sponsor applied to or part of the PRIME programme at EMA

History of submitting topics for joint HTA (EUnetHTA)

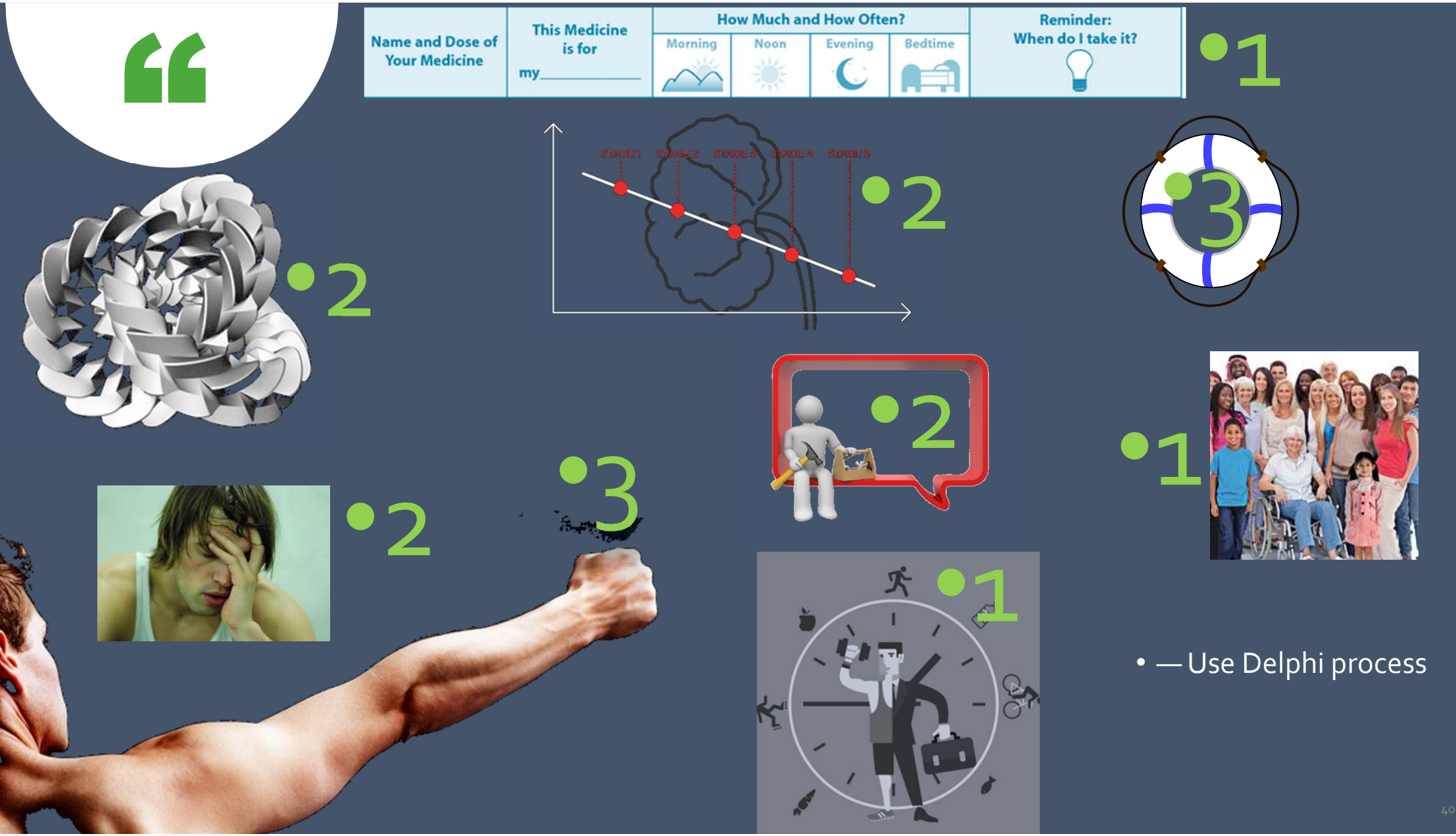
No record of bad practice

Which sponsors should be priority? (in addition to medical interest)

• Third step

Weigh your criteria and prioritise

And adjust when new information comes in


Name and Dose of Your Medicine
This Medicine is for
my_____
How Much and How Often?
Morning
Noon
Evening
Bedtime
Reminder: When do I take it?
1
2
STAGE 1
STAGE 2
STAGE 3
STAGE 4
STAGE 5
2
3
2
2
1
2
3
1
• — Use Delphi process

application

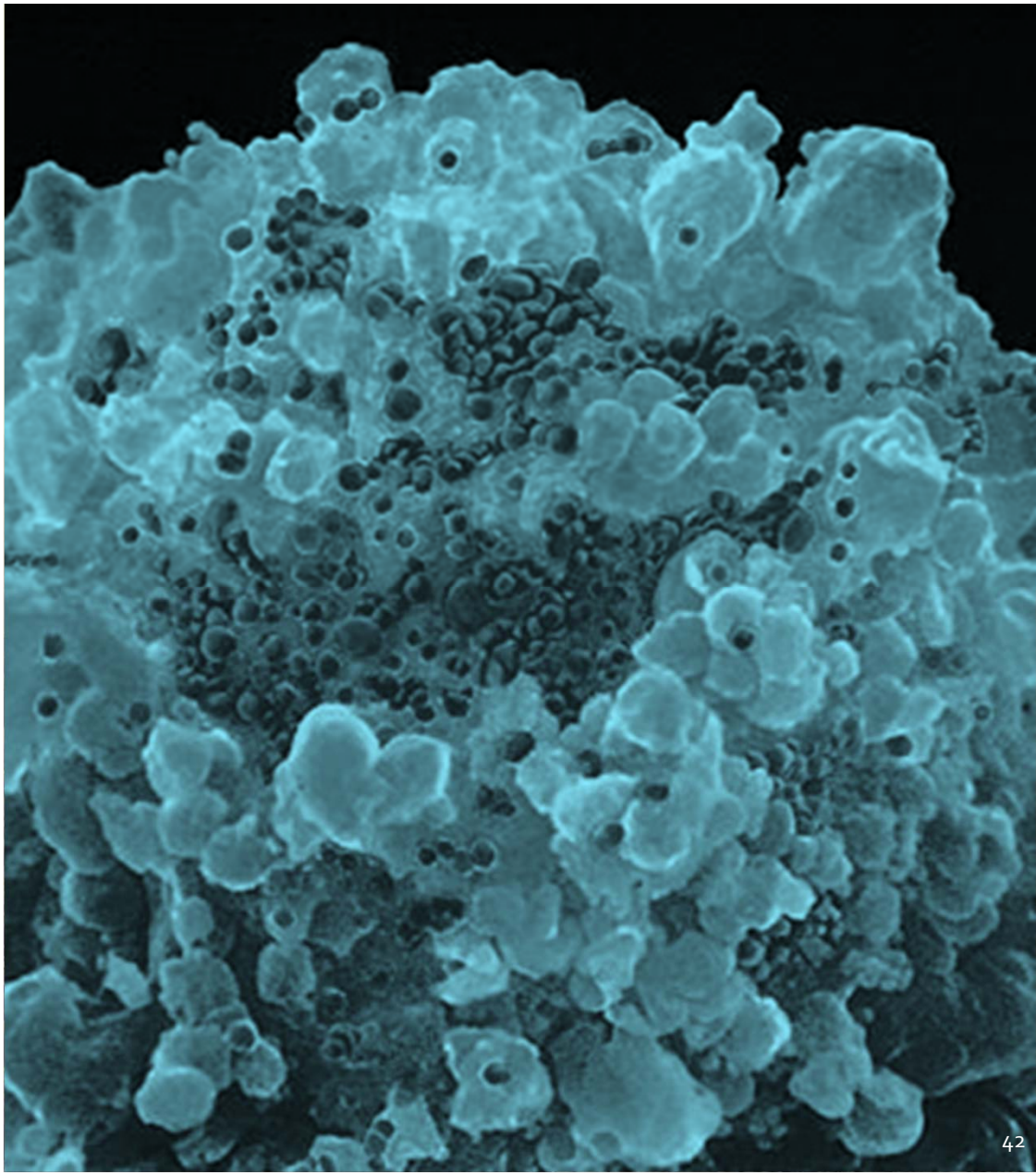
HIV pipeline in 1999

- **130 compounds in R&D in 1999**

- Systematic review

Selection of 18 of particular interest

- Community Advisory Boards: regular meetings with their developers
  - **Efficient?**



- **130 compounds in R&D**
  - A step by step process

Based on which criteria?

•illustration

- Overall it represents a comprehensive analysis

ENGAGE

- With developers to obtain data
  - **Share results with regulators**
  - Or HTA, payers

	F-ddA	PMPA	Tipranavir / r	ABT 378/r	d-APD	T20 & T1249	IL2	DOTC
Class (target)	Reverse transcript. Inhibitor RTI	Reverse transcript. Inhibitor RTI	Protease inhibitor PI	Protease inhibitor PI	Reverse transcript. Inhibitor RTI	Fusion inhibitor FI	Immune therapy	Reverse transcript. Inhibitor RTI
Class (chemical)	Dideoxy-purine nucleoside similar to ddA NRTI	Nucleotide analogue NtRTI	Non peptidic protease inhibitor	Peptido-mimetic protease inhibitor	purine nucleoside analogue NRTI	Amino-peptide	peptide	2'-deoxy-3'-oxa-4'-thiocytidine nucleoside analogue NRTI
Susceptibility of mutated strains R:resistant S: sensitive	S except MDR strains	S	S	S beavily pretreated patients ?	S	S	NA	S
Genetic barrier	High	High	High	High	?	Low for T20		?
safety & tolerance	?	Safe so far, but kidneys ?	Safe so far. GI tract. metabolic disorders ?	Safe so far. GI tract. metabolic disorders ?	?			
Potency (monotherapy)	≅ -0.44 log (in pretreated patients)	≅ -1.25 log	≅ - 1.8 log	≅ - 2 log	?	≅ - 1.2 log		≅ - 1 log
Favourable profile for salvage regimens according to data currently available								
# daily intakes and administration								
daily dose	300 to 400 mg	150, 300 or 600 mg		800/200				
pills / day	1 pill	1 to 2 (75, 150 and 300 mg tablets)		6				
Special precautions								
# patients exposed as of 1 October 1999	187	193						
Development phase (current)	II	II/III	II	III	I	I	III	II

To treat the Human Immune-deficiency Virus Infection

European AIDS Treatment Group e.V.
Mindenerstr. 33 D-40227 Duesseldorf
Germany

Research & Development

Future therapeutic options for patients: an overview.

Author: François Houÿez

Thank you to:

Goncalo Dinis (Portugal)

Simon Collins (Royaume Uni)

Lital Hollander (Italie)

Conny Loosen (Germany)

•Of the 18 selected

- 9 were authorised
- 1 was rejected, on patients' request
- 8 failed to show benefit

No product was authorised, which had not been scanned by the CAB

- Filtration: 86% (not selected / all)
- Sensitivity: 56% (prob. MAA if selected)
- Specificity: 100% (Prob. no MAA if not selected)

Authorised	In	Anticipation (months)
abacavir	08/07/1999	24
amprenavir	20/10/2000	36
Didanosine enterocoated	22/02/2000	28
lopinavir	20/03/2001	41
tenofovir	05/02/2002	52
emtricitabine	24/10/2003	72
enfuvirtide	27/05/2003	67
atazanavir	02/03/2004	77
tipranavir	25/10/2005	96
average		55

EATG recommended not to authorise it (FDA public hearing)
Adefovir dipivoxil

Failed (lack of efficacy, or safety issue)	
D-OTC	Remune
Interleukine 2	F-ddA
Delavirdine	DPC961
DPC963	emivirine

- — EATG Horizon Scanning efficacy

- As done by LBI in Austria 2008

•1

Table 3.4-1: Criteria for Priority Setting

criterion	answer options	score
1) When does the technology appear likely to be launched in Austria/in the EU?	it is already available/adopted	0
	in 0-2 years	2
	in 2-4 years	1
	in 4 or more years	0
2) Burden (severity) of disease (mortality, morbidity, quality of life)	high	2
	moderate	1
	low	0
	unknown	0
3) Estimated number of patients with disease in Austria (per year)	more than 1000	3
	500-1000	2
	100-500	1
	0-100	0
4) Is this an innovative drug for a disease with no satisfactory standard treatment?	yes	2
	no	0
	don't know	1

Geiger-Gritsch Sabine. Horizon Scanning in Oncology – Concept Development for the Preparation of a Horizon Scanning System in Austria. HTA Project Report 2008; 14.

- As done by LBI in Austria 2008

•2

5) Is there potential for a significant health benefit to the patient group (high clinical impact)?	major	2
	moderate	1
	minor	0
	unknown	0
6) Is there potential for a significant impact on hospital drug budgets if the technology diffuses widely (because of expected moderate to high unit costs and/or because of high patient numbers)?	major	2
	moderate	1
	minor	0
	unknown	0
7) Is there potential for inappropriate diffusion (too fast or too slow) or use (off-label) of the technology?	major	2
	moderate	1
	minor	0
	unknown	0

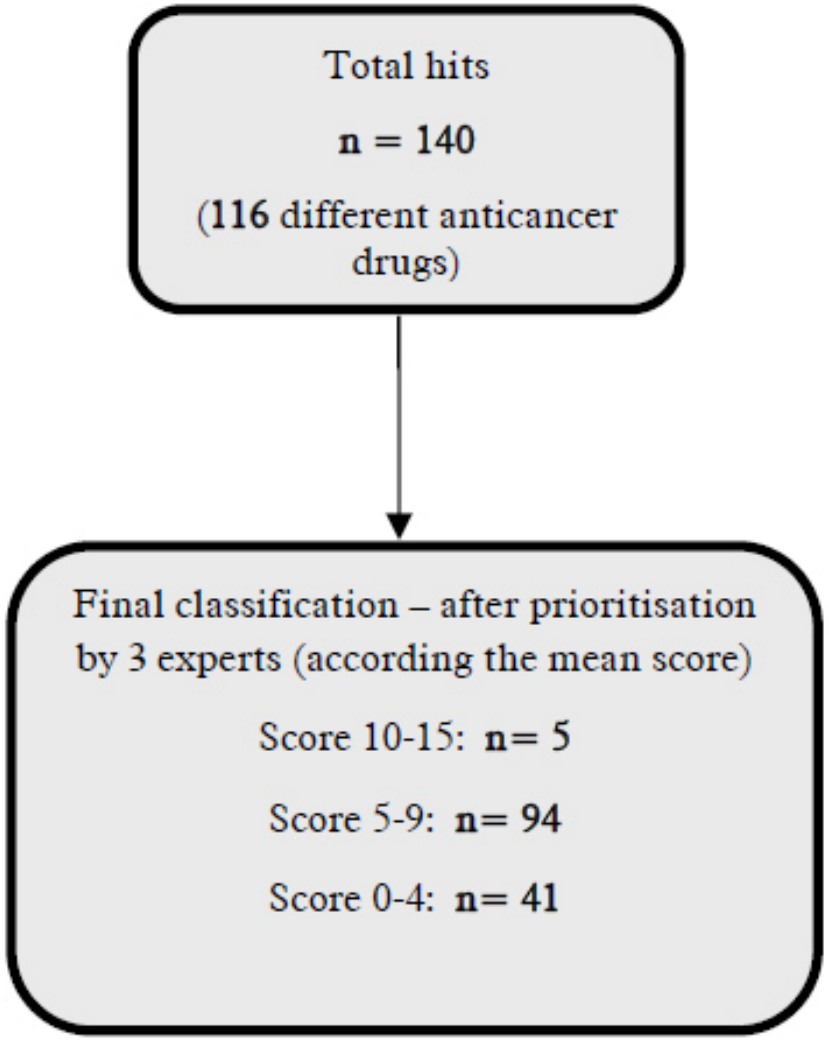


Figure 3.5-1: Results of the prioritisation process

- **3**
- prioritisation

3 experts asked to rank the 140 proposed product/indication pairs

3 oncology experts asked to rank according to criteria

- **5 products with highest scores (10 to 15)**

• **Denosumab prostate Kr**	• **Motesanib for NSCLC**	• **Vandetanib lung cancer**	• **Cetuximab lung cancer**	• **Afatinib NSCLC**
• Expert 1: 13	• Expert 1: 11	• Expert 1: 10	• Expert 1: 12	• Expert 1: 10
• Expert 2: 13	• Expert 2: 14	• Expert 2: 15	• Expert 2: 15	• Expert 2: 14
• Expert 3: 5	• Expert 3: 5	• Expert 3: 5	• Expert 3: 6	• Expert 3: 5
• MA: not for this cancer	• Abandoned	• MA: not for this cancer	• MA: not for this cancer	• MA: 25/09/2013 (3 years later)

- François Houÿez
- Rob Camp
- francois.houyez@eurordis.org
- rob.camp@eurordis.org

Now it's up to you to scan!

THANK YOU