

Sulfateq B.V.

Drug Development company

CEO A.C. van der Graaf



Science to the market

The cooperation SME and University on innovation and transfer technologies.

- Introduction
 - > World of Large companies and SME
 - > Innovation in which Field
- General Innovations
- Pharma
- Advise what has worked BIOBRUG (BioBridge)
- My story

Innovation

- Large Company
 - > Innovation initiated by
 - Strategic survey
 - Need to go in new fields or extend existing
 - Expansion of existing Product line
 - > To survive in a large company Politics is essential
 - > Politics and innovation could be conflicting
 - > Burocrazy
- SME
 - > Innovation by seeing possibilities

Differences

- Large companies
 - > Have a real budget
 - > Have access to the brightest persons
 - > Have access to a large network of knowledge based institutions
 - > Have access to license patents
 - > Internal politics and Persons goal to gain better position in 4 years.
- SME
 - > Limited resources
 - > A vision and a will to gain success
 - > Are Naive

Innovation field general remarks

- Electronics

- > The law of Moore every 2 year double capacity of chips
- > Innovation could be scheduled by these facts

- Pharma

- > Innovations of a known cure

- Make a me too e.g. different forms of Statines
- Extension of known principles e.g. Antibodies recombinant proteins

- > Large innovations nothing predictable

- Large Pharme buys actively a proven concept

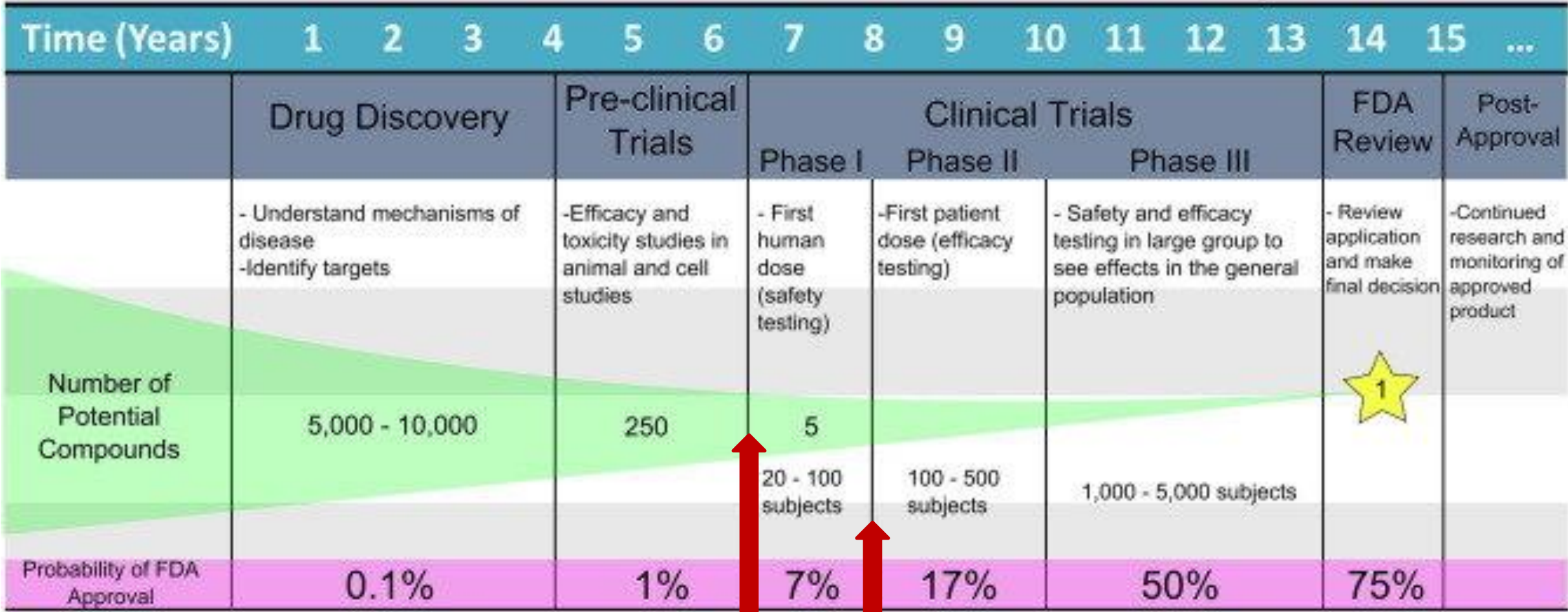
Pharma innovations

- Source in most cases is science from universities
 - > Demand for specific diseases (clinical observations)
 - > New working mechanism (medical biology /chemistry)
 - > Conceptual thoughts
- One observation / good idea is not a product **Development is needed**
- Working with different fields of knowledge is not realistic in University
 - > Every research group has goals to publish, that is not a product for sale
 - > Research group work together, but are not flexible
 - > Research groups are based on budgets mostly have no open funds
- **An SME is then the best option for Development process**

SME in Pharma development Criteria

- Being flexible and pragmatic
- Cooperation with academic persons and have full trust together during long time
- Possible profits and costs must be contracted before starting
 - > the institutions
 - > transparant with persons in academia
- The SME use other academic groups to obtain results during the process
- Cash of SME
 - > Investors
 - > Grants, non diluted funds

Overview development SUL-238 as therapeutic for Alzheimer's Disease



Today Q3, 2023



One of the succes factors

- Bio Brug Method (Bio-bridge)
- Local SME work with academic groups, a defined project e.g. a Proof of Concept of the drug
- Financed by grants e.g. Local and diminish cost in university, **Low cost SME**
- When the result is positive, then a patent, **owner of patent the SME**

Result

- SME obtain patent, **cost of the patent are for the SME**
- University group develop new fields of expertise,
> due to focussed question of SME
- Local SME and University persons with future expansion possibilities

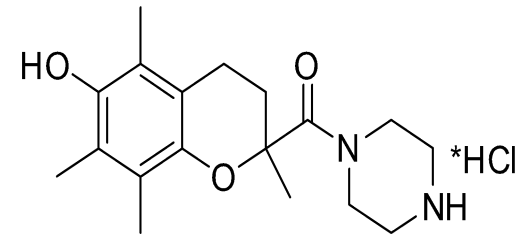
Sulfateq Case

- First conceptual thoughts: **Hybernation** Prof Rob Henning & Dr Anne Epema
- First some simple experiments at university (2010 -2011)
- Set up Sulfateq 2011
 - > Stakeholders friendly investors, and Holding company university
 - > Contract with University: a defined amount if success is achieved
- Start with development of compounds and test them in cell based assays
- Define applications: first storage of blood platelets, later Drug development
- Strong Active compounds into several Animal models Proof of Concept
- Set up of Chemistry and toxicology program
- Partnering by licensing out one application: Neurodegenerative Disease
- Further development to drug

Frontrunner Compounds

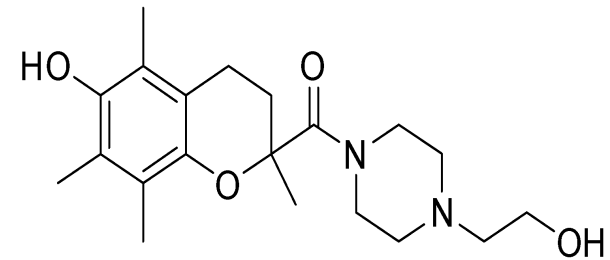
SUL-121 racemic mixture:

- SUL-150
- SUL-151



SUL-109 racemic mixture:

- SUL-132
- SUL-138
- SUL-238 = SUL138 HCL salt

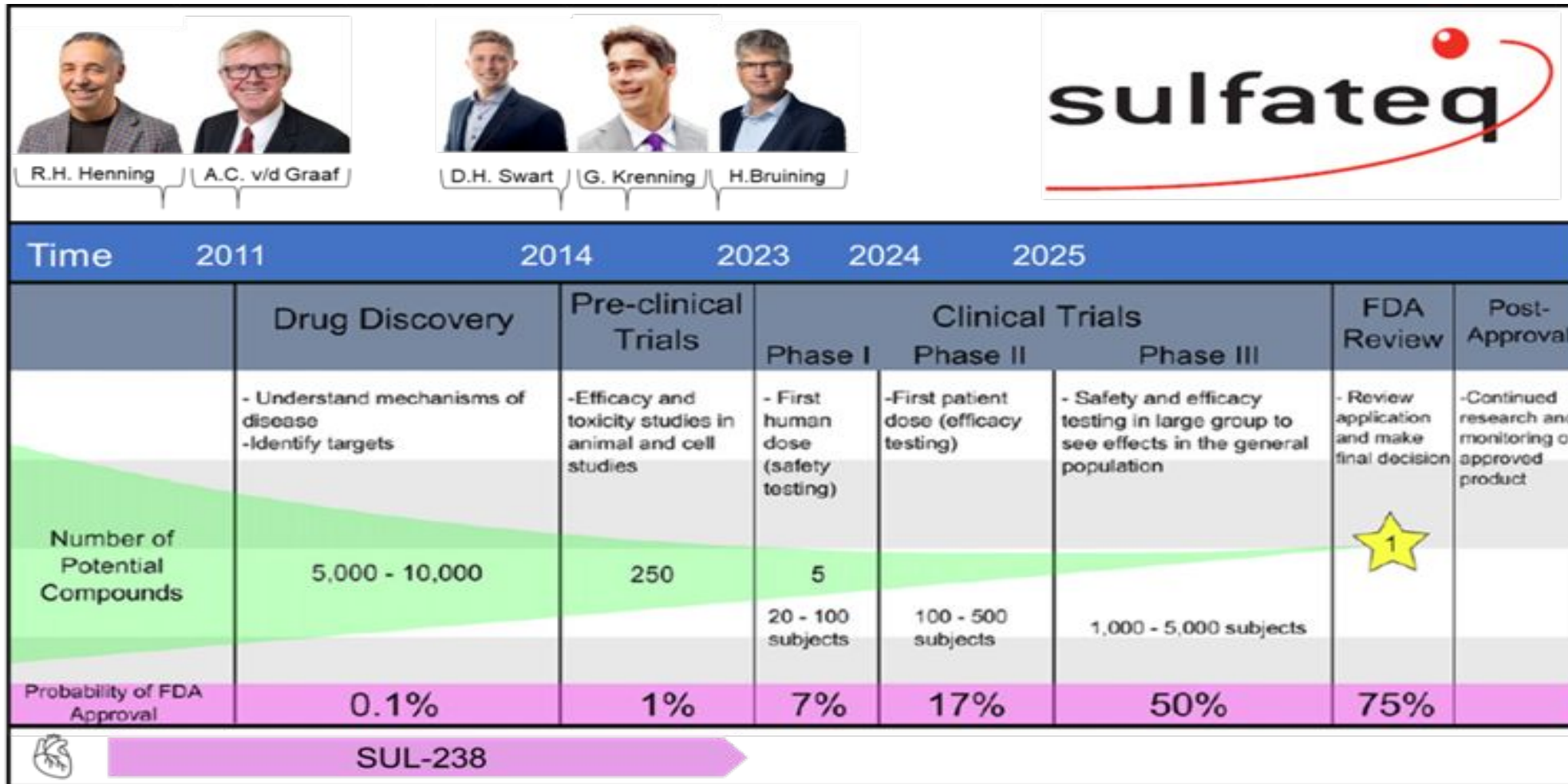


Sulfateq's pipeline

Product portfolio of innovative mitochondria-targeted small molecules



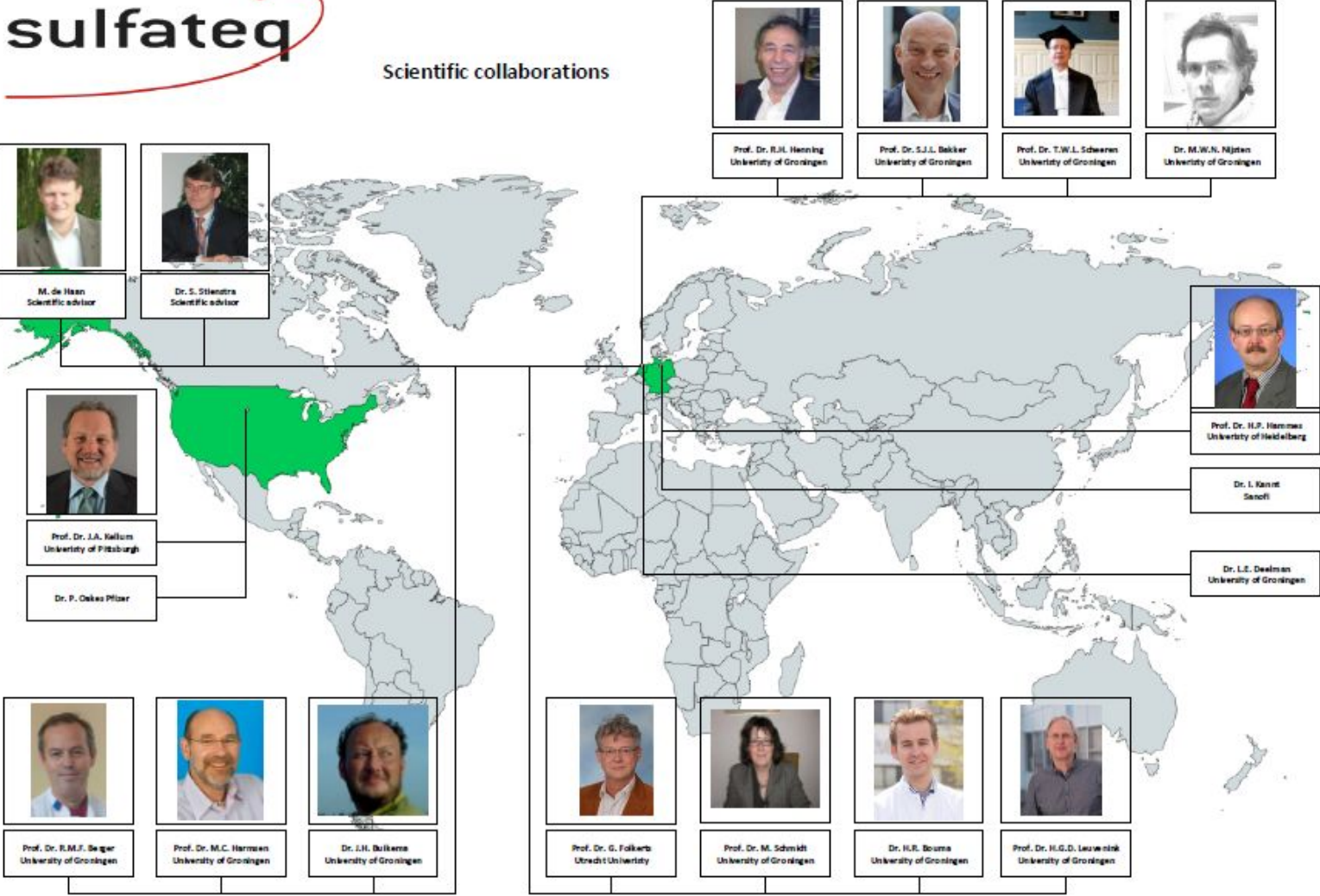
Development SUL-238 and joining of key personnel



Overview academic network Sulfateq



Scientific collaborations



Summary

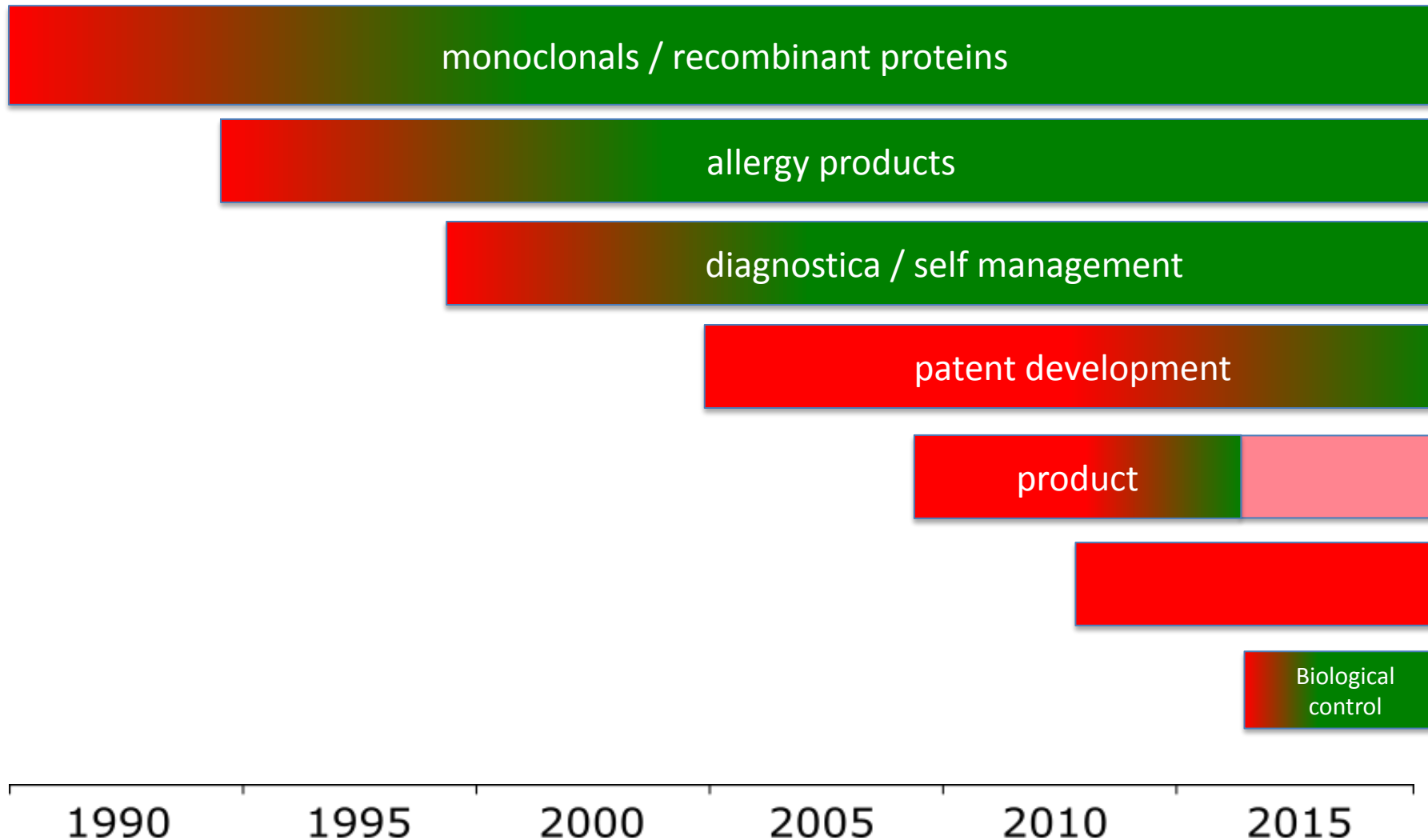
- Sulfateq active in drug development for Mitochondrial diseases
 - > Mitochondrial diseases occur when mitochondria fail to produce enough energy for the body to function properly.
- Sulfateq has built a successful platform of small molecule drugs targeting mitochondrial diseases in various stages of development and approval
- Sulfateq has a proven track record of early stage partnering and taking products through to commercialization
- SUL-238 expected to end Fase I successfully in Q2-3 2023
- After Fase I, direct start Fase 2-a
- This will develop revenues for new compound investment

Sulfateq activities

- Own research in laboratory
- External Chemistry
 - > Based on this internal chemistry production
- Broad contact range in experts and University groups
- Internal
 - > Production e.g. of compounds , specific research developments
 - > Project management
 - > Financial set up and very cash driven
 - > Pragmatic and Creative with sourcing
 - > Searching Pharma Partners

Kees van der Graaf

Core business: product development Science to the Market



Bio-Intermediair

CITEQ
biologics

sanelco

angteq

Nyken
THERAPEUTICS

17

sulfateq

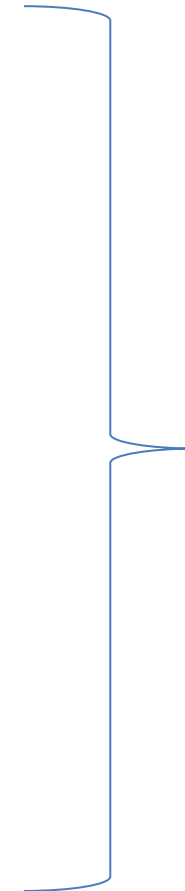
Tryptomera
Specialist in Bodemroofmijt

sulfateq



Achivement of SME Sulfateq

- General chemistry
- Medicinal Chemistry
- Biology,
- Cell culture
- Enzymes
- the business side of biopharma,
 - > Managing
 - > Working Team
- patent issues,



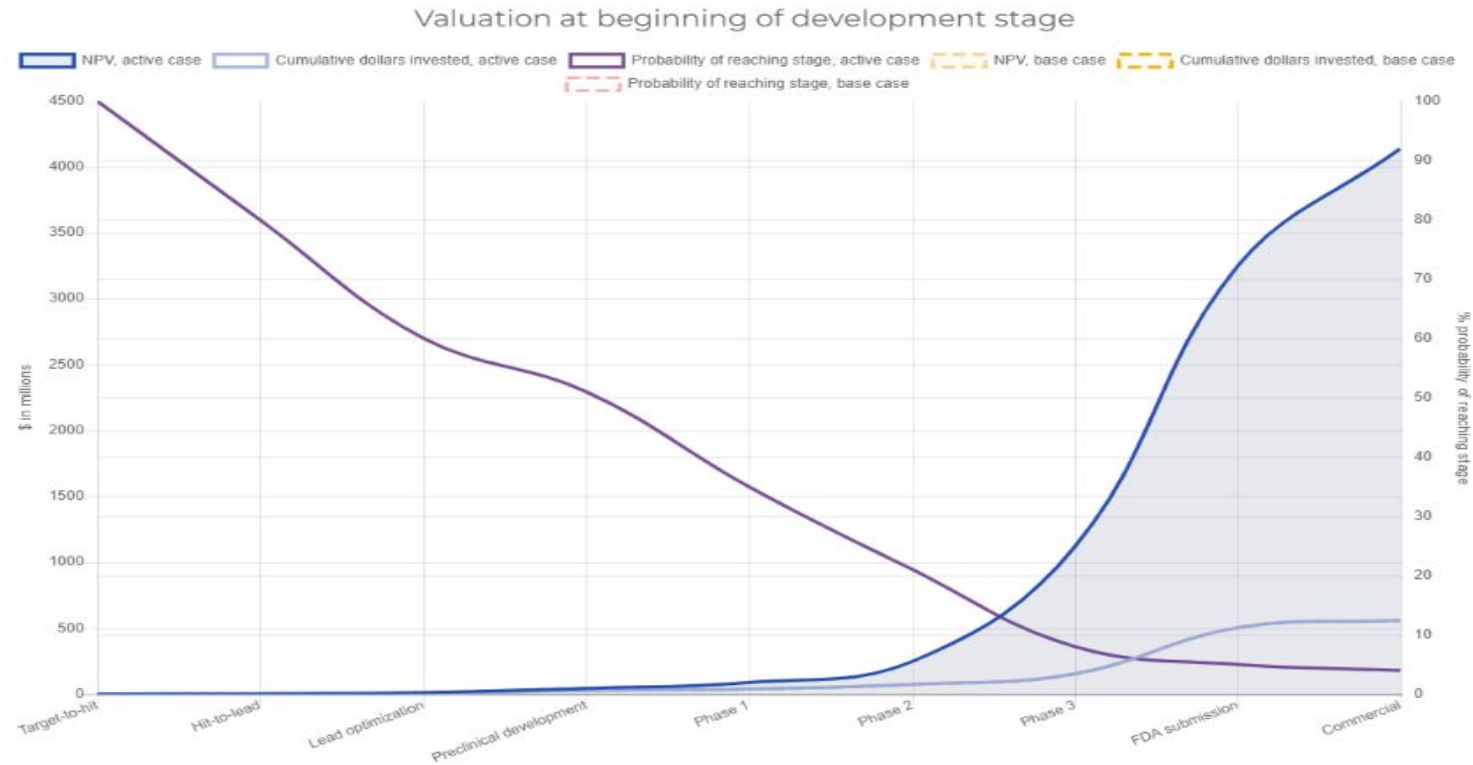
History of Sulfateq B.V.

- 2011 Establishment Sulfateq B.V.
(Shareholders: Turftoren Beheer BV, Citeq BV and small)
- 2011 – 2014 Backbone screening, library development, in vitro screening, ADME
- 2015 – 2019 Preclinical proof of concept in various animal models
- 2020 Choice for SUL-238 as most promising compound
- 2021 SUL-238 for Neurodegenerative diseases licensed to **GEN Iliac**, Ankara (GEN has a financial commitment for the development Phase I, Data are fully available for Sulfateq)

Sulfateq holds freedom-to-operate in all other disease areas

- 2022 Phase I is planned for November 2022
- 2023 Phase II-A scheduled for Q3/Q4 2023

Value model SUL-238 through different stages of development



Value at start of program

\$0M

Probability of FDA approval: 4%

Investment required for approval:
\$559M

Value at start of Phase 1

\$88M

Probability of FDA approval: 12%

Investment required for approval:
\$520M

Value at start of Phase 2

\$248M

Probability of FDA approval: 20%

Investment required for approval:
\$486M

Value at start of Phase 3

\$1,119M

Probability of FDA approval: 56%

Investment required for approval:
\$405M

Total pharma market 2020

- Total Pharma Market \$ 1,27 trillion
- Total Pharma R&D \$ 190 billion (14 % of turnover)
- No 1 Sales of product Humira (AbbVie) \$ 20,4 billion
- Largest R&D spending Merck (MSD) \$ 13,6 billion
- 12 companies R&D > \$ 5 billion
- Pharma M and A amount (PWC 2022)\$ 350-400 billion

Phases I- 4

- small compounds □ 1541 studies in total,
- **503** in phase I (of which 234 completed and 52 terminated/withdrawn),
- **549** in phase 2 (of which 198 completed and 84 terminated/withdrawn),
- **123** in phase 3 (of which 57 completed and 13 terminated/withdrawn)
- **50** in phase 4 (of which 30 completed and 3 terminated/withdrawn.
- **298** studies the phase was not applicable, of these 167 are completed and 11 terminated/withdrawn.
- <https://clinicaltrials.gov/ct2/results?cond=&term=small+molecule+OR+small+compound&cntry=&state=&city=&dist=>

- **RESULTS** registered annually 15-42

Pharmaceutical Total Sales Per Product worldwide Number 1- 50

Medication	Company	Price l
• 1. Humira (Adalimumab)	AbbVie	\$19.9 billion \$
> \$5,243 for 80 mg Rheumatic Diseases and Inflammatory Bowel Disease		
• 49. Aubagio (Teriflunomide)	Sanofi	\$1.94 billion
> \$6,904 for 28 pills Multiple Sclerosis		
• 50. Aranesp (Darbepoetin Alfa)	Amgen	\$1.88 billion
> \$3,073 for 400 mcg Anemia		

<https://truecostofhealthcare.org/pharmas-50-best-sellers/> 2018

~~Computation of the market~~ Market computation of a product e.g. Alzheimer

- e.g. Alzheimer
 - > Number of high-income people in the World = 2 billion people
 - > 5% of high-income people is older than 80 years, = 100 million people
 - 30% of people above 80 years has Alzheimer, in different forms
 - Potential of 30 million high-income patients
 - Alzheimer cure costs approx. € 2-3 per day. ~~is yearly~~ Annual cost per patient is € 1000,-
 - ~~sales to~~ 33 % sales to high-income people above 80 represents 10 million persons. (~~0,5 % total population~~)
 - > Potential Annual Market Value > € 10 billion
- This figures can be computed with: Heart Failure, COPD, CKD

Pharma companies R&D in 2020

2020 PHARMA 50 - R&D SPENDING RANK	COMPANY	R&D SPEND
1	Merck	\$13,558,000,000
2	Roche Pharmaceuticals (division of Roche Group)	\$12,164,234,743
3	Bristol Myers Squibb	\$11,143,000,000
4	Janssen (Johnson & Johnson's pharmaceutical segment)	\$9,563,000,000
5	Pfizer	\$9,405,000,000
6	Novartis	\$8,980,000,000
7	AbbVie	\$6,557,000,000
8	GlaxoSmithKline (GSK)	\$6,509,126,400
9	Sanofi	\$6,303,060,000
10	Eli Lilly	\$6,086,000,000
11	AstraZeneca	\$5,991,000,000
12	Gilead Sciences	\$5,039,000,000
13	Takeda Pharmaceutical	\$4,611,350,440
14	Amgen	\$4,207,000,000
15	Biogen	\$3,990,900,000
16	Boehringer Ingelheim	\$3,245,614,035
17	Bayer (Pharmaceuticals Division)	\$3,127,020,000
18	Regeneron Pharmaceuticals	\$2,735,000,000
19	Novo Nordisk	\$2,368,105,810
20	Incyte	\$2,215,942,000