



Bioloogiliste ravimite arendus Icosagenis ja keemikute roll selles tegevuses.

**Mart Ustav
Icosagen Grupi juhataja**

2023 Confidential

DOB 16.07.1949

Curriculum vitae Mart Ustav, Sen.

1. Education – Organic and Bioorganic Chemistry, 1972, Univ. Of Tartu
2. First job: Institute of Cybernetics, Tallinn – researcher, enzyme kinetics 1974
3. Ph.D. – rRNA-protein interactions, Univ. of Tartu, 1976-1979
4. Post-doctoral Fellow – Uppsala University 1982-1985
5. Head of Laboratory of Oncogenesis, EBC 1985-2001
6. Visiting scientist – Cold Spring Harbour Laboratory, Long Island, NY, USA (1989-1992)
7. Professor of Microbiology and Virology 1992-2007, Univ. of Tartu
8. Director of the Institute of Molecular and Cell Biology 1996-1999
9. Howard Hughes Medical Institute Fellow, USA 1995-2005
10. Member of the Academy of Sciences of Estonia 2001
11. Professor of Biomedical Technology 2007-2021. Since 2021 Professor Emeritus TUIT.
12. Director of the Institute of Technology, University of Tartu, 2002-2007, 2012-2017
13. Founder and CSO – FIT Biotech Eesti AS 2001-2011; Chairman of the Board Quattromed AS (1999 -2008)
14. Founder and CEO, Icosagen Group (Icosagen AS, Icosagen Cell Factory OÜ, Ico Park OÜ, Icosagen Technology Inc.) Since 2008. Confidential



The first 10-years of Icosagen as Quattromed

1999

- **Quattromed** was founded as a **molecular diagnostic company** for providing services to Estonian medical institutions. 2001 FIT Biotech Oy acquired 22.3% of the Quattromed shares and established FIT Biotech Oy Eesti filiaal

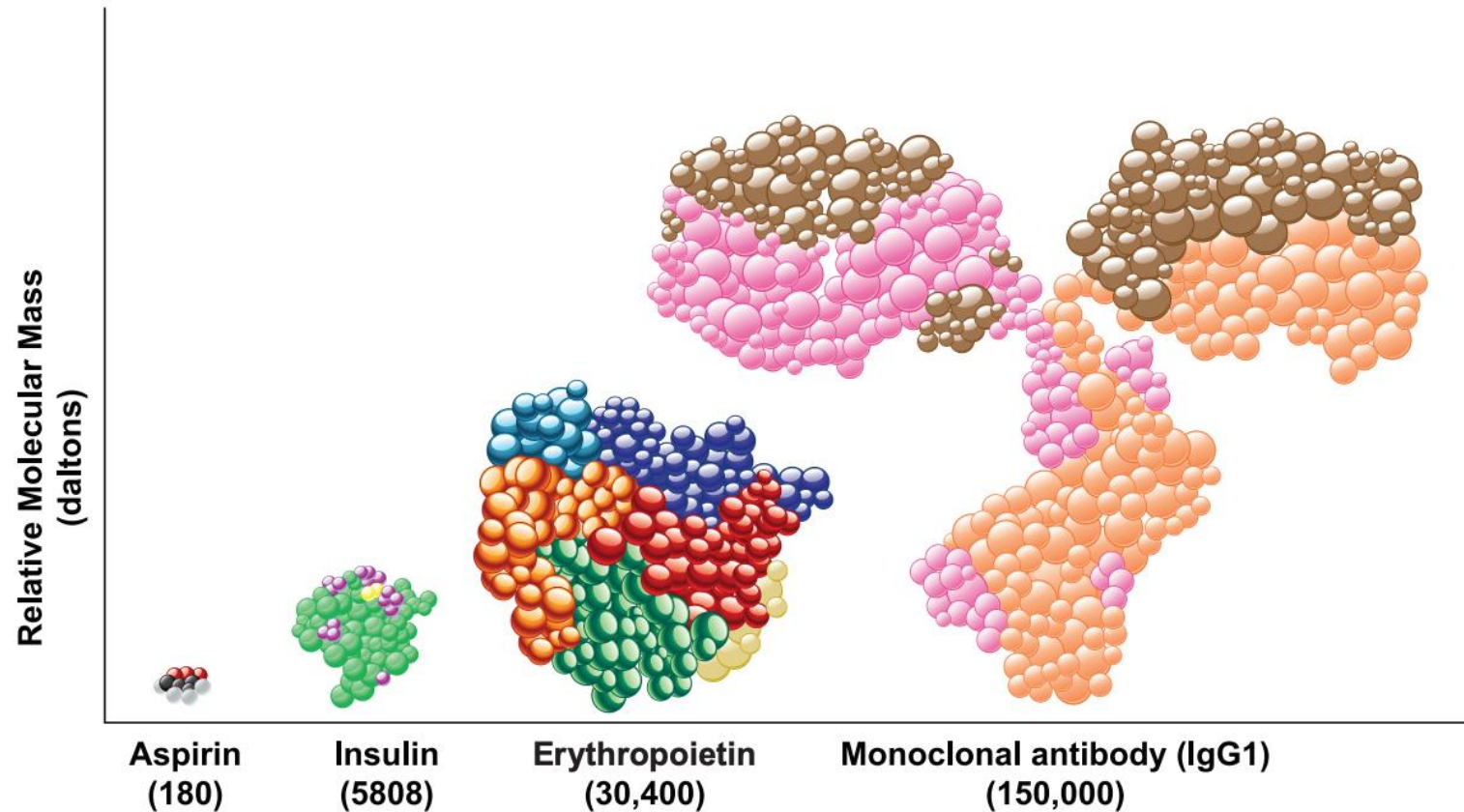
2005

- Diversification of medical services and establishment of Quattromed Cell Factory as a subsidiary company

2008

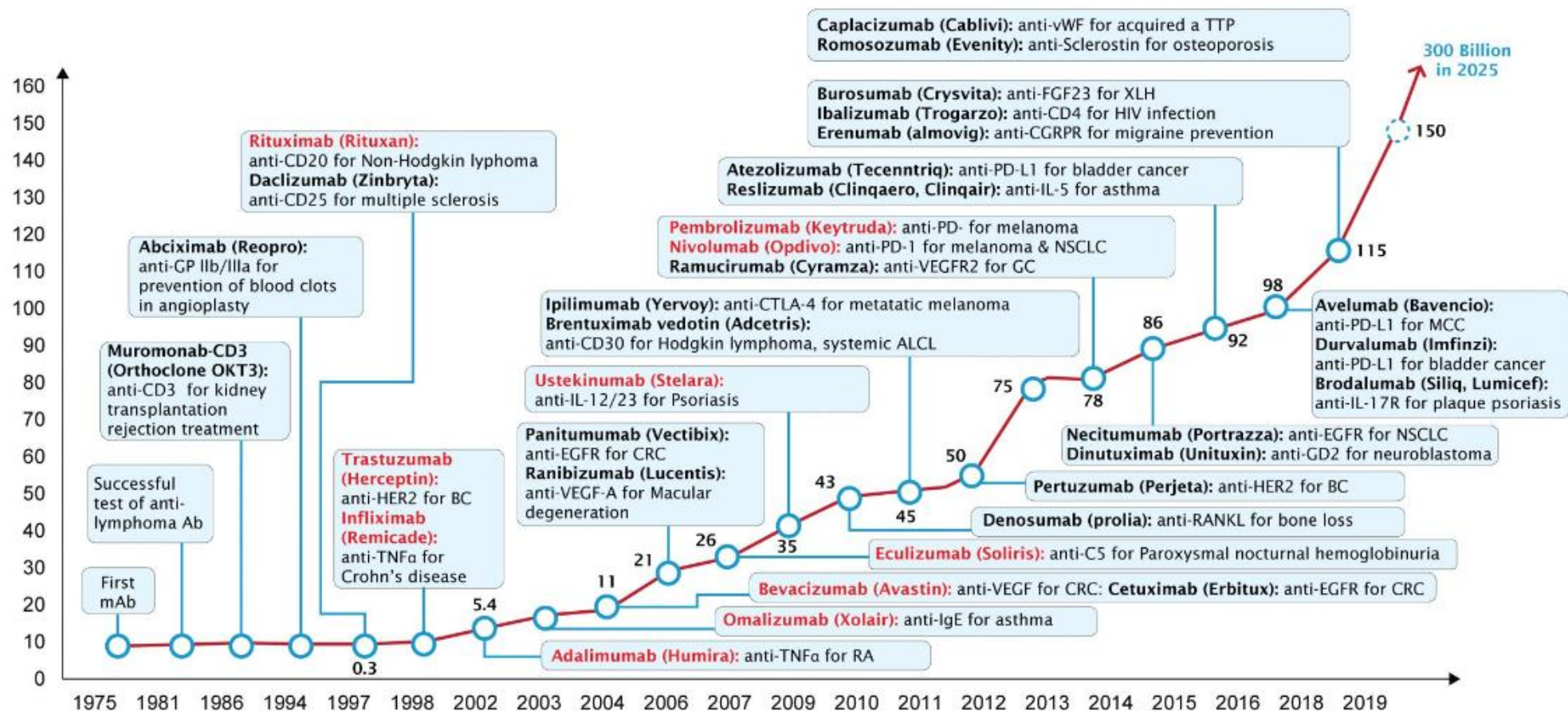
- A leading medical diagnostics and biotechnology group in Estonia, **80 FTE; service labs in several cities; revenue EUR 4.5 MEUR**
- **Activities:**
 - medical diagnostics: molecular diagnostics, clinical chemistry, hematology, cytology, immunology etc
 - molecular- and cell biology products and services
 - immunoanalysis products and services for detection of allergic causativ proteins in rubber products
- **Q3:** the medical diagnostic subsidiary along the trademark Quattromed was sold to private equity firm. Restructuring of the group and business model.
- Establishment of Icosagen Group inn 2009

Biologic drugs are high molecular weight complex molecules



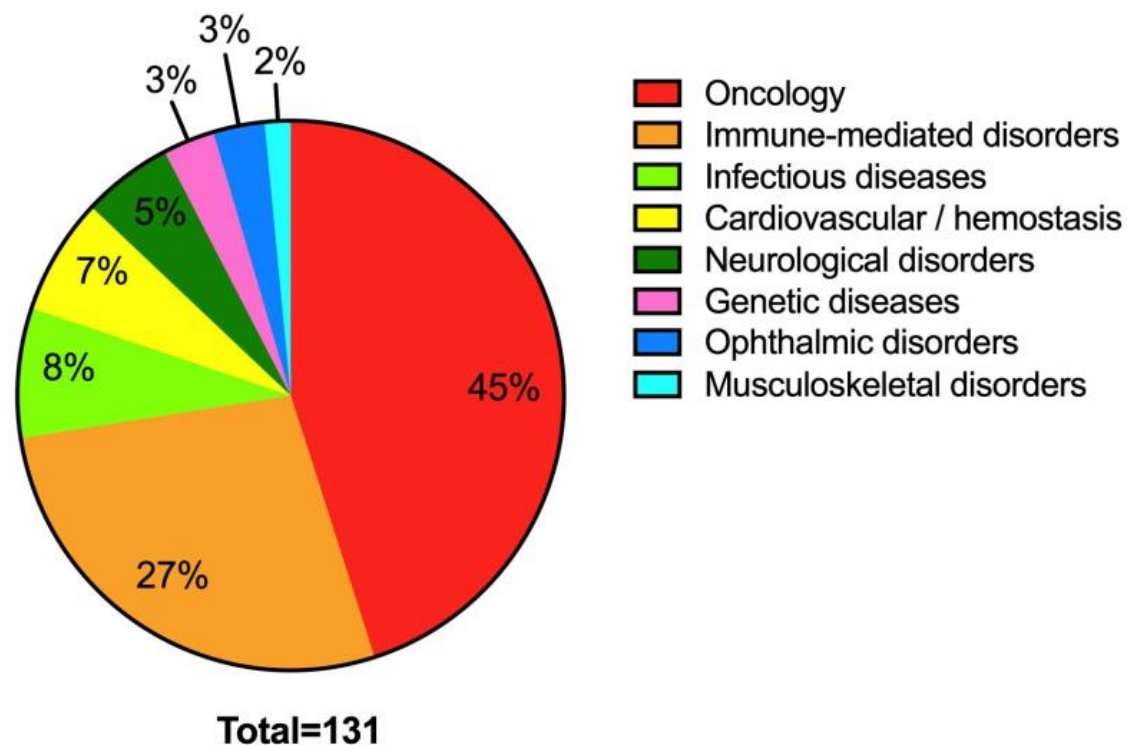
Mellstedt H. Clinical considerations for biosimilar antibodies. EJC Suppl. 2013 Dec;11(3):1-11.
doi: 10.1016/S1359-6349(13)70001-6. PMID: 26217160; PMCID: PMC4048039.

Antibody drugs are highest selling drugs



Lu, RM., Hwang, YC., Liu, JJ. *et al.* Development of therapeutic antibodies for the treatment of diseases. *J Biomed Sci* **27**, 1 (2020). <https://doi.org/10.1186/s12929-019-0592-z>

Biologic drugs are highest selling drugs



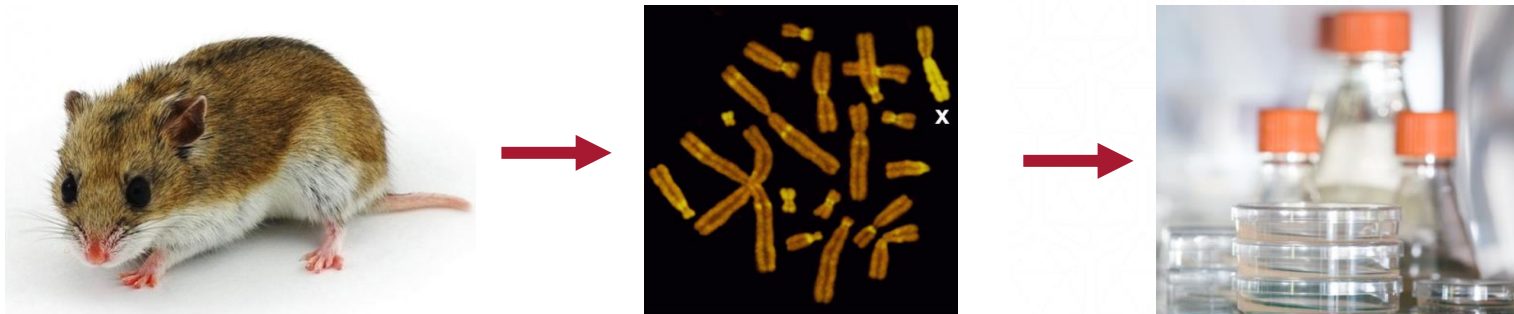
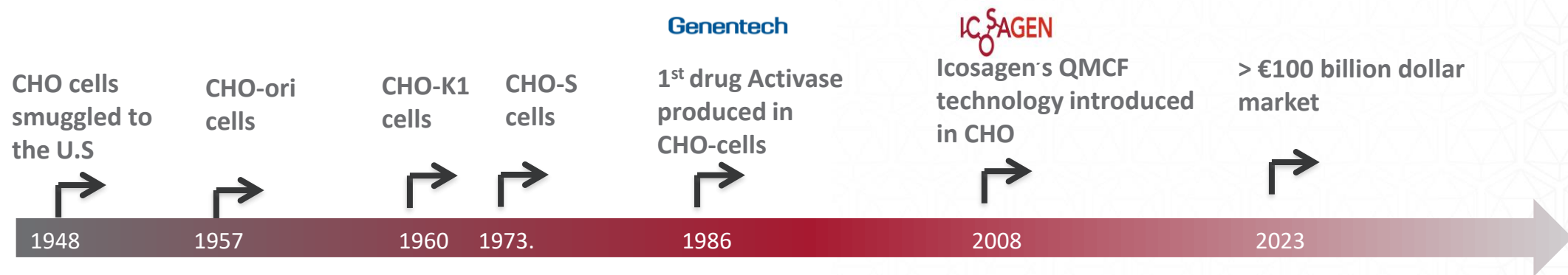
Top-10 selling drugs in 2021

Drug's name	Manufacturer	Estimated sales in B\$ (2021)	Drug type
Comirnaty	BioNTech/Pfizer	36	Vaccine
Humira	AbbVie	20	Antibody
Keytruda	Merck & Co	17	Antibody
Spikevax	Moderna	15	Vaccine
Revlimid	BMS	13	Small molecule
Eliquis	BMS/Pfizer	11	Small molecule
Imbruvica	J&J/AbbVie	10	Small molecule
Eylea	Regeneron/Bayer	9	Recombinant fusion protein
Stelara	J&J	9	Antibody
Biktarvy	Gilead	8	Small molecule

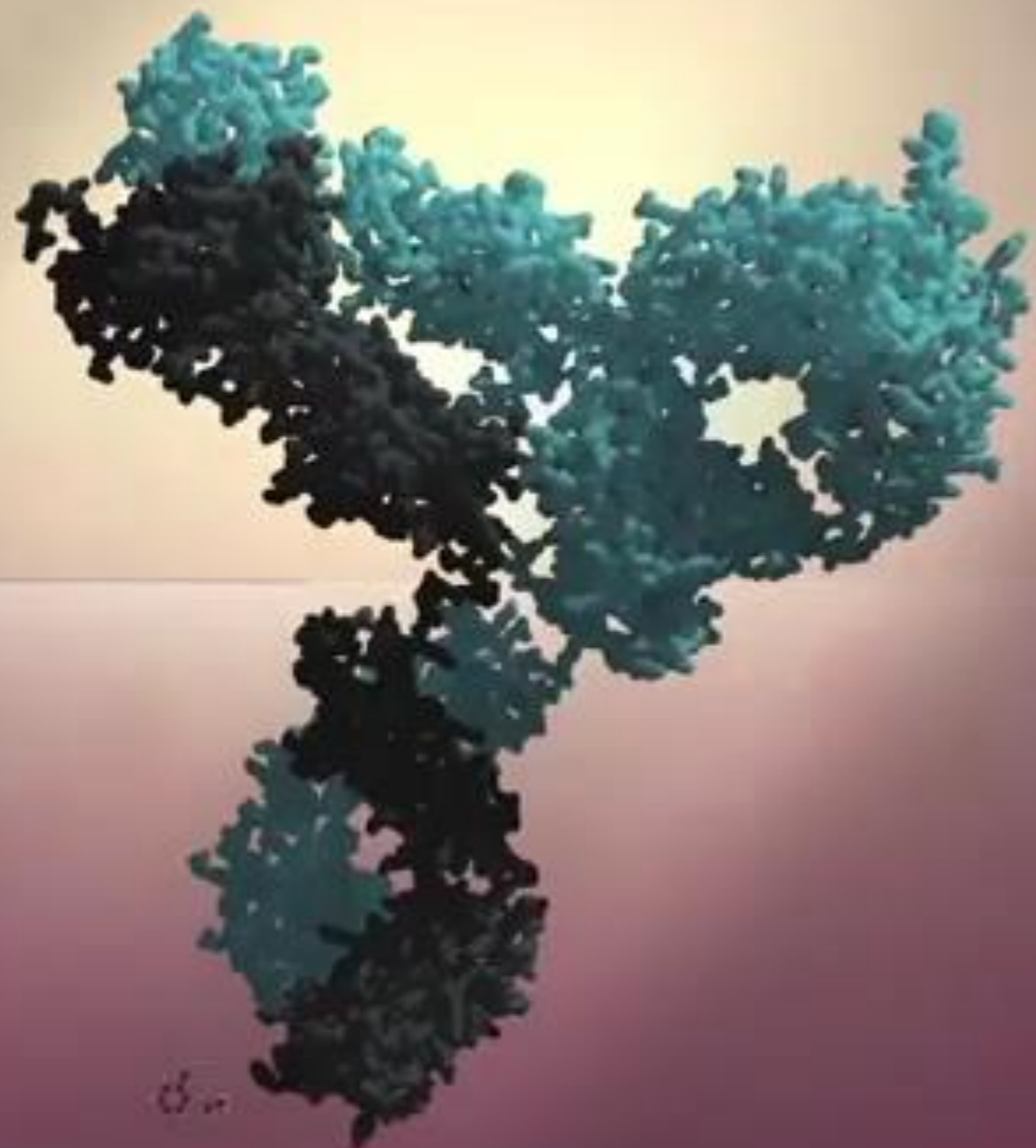
NASDAQ

Therapeutic antibodies are produced using Chinese Hamster Ovary (CHO) cells as cell factories.

>100 billion EUR worth of biologic drugs are produced in CHO cells annually



1000x
AS LARGE AS
SMALL MOLECULE DRUGS



Icosagen Group

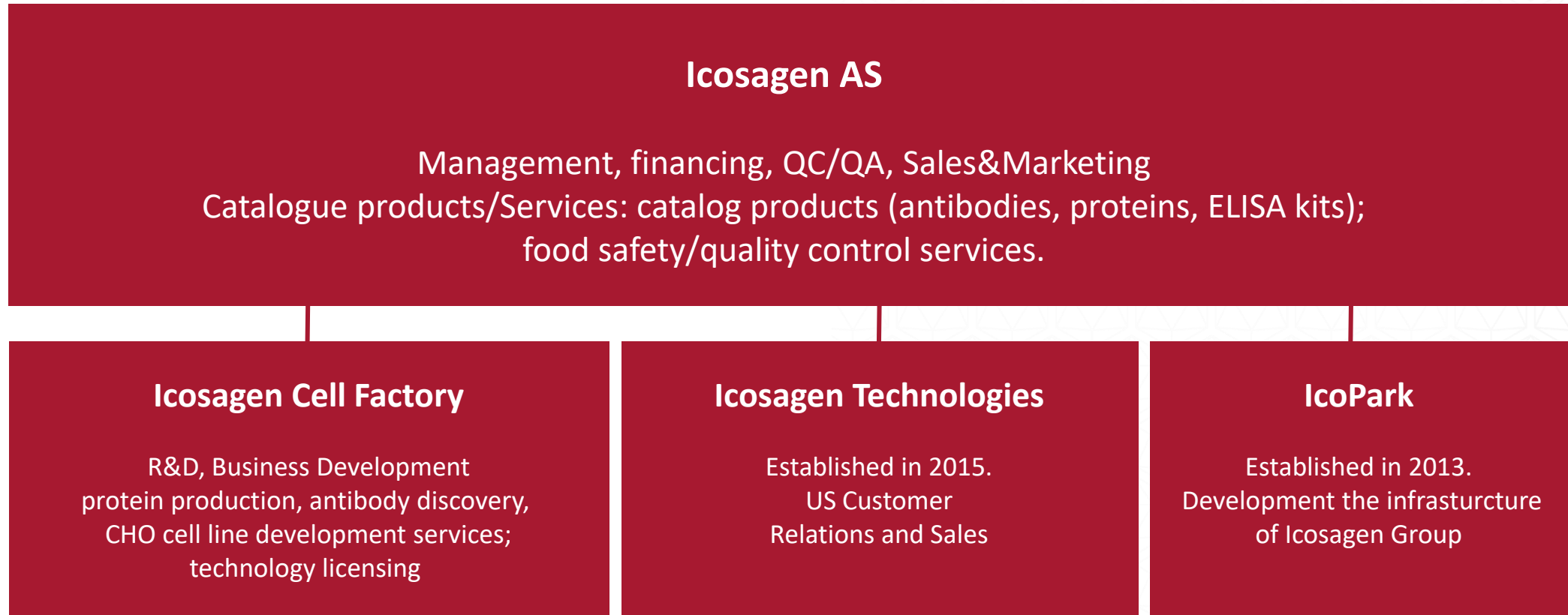
- Discovers, develops and manufactures mammalian protein drug candidates
- From R&D concepts to clinical development stages
- 180+ FTEs (38 PhD)
- ISO 9001:2015, ISO 17025
- >25 patents in 7 families (EU, US, CA, JP, AU)
- 6200m² lab & office space, 300m² animal facility
- 50L, 200L, 1000L single-use GMP bioreactors



San Francisco
USA

Tartu
ESTONIA

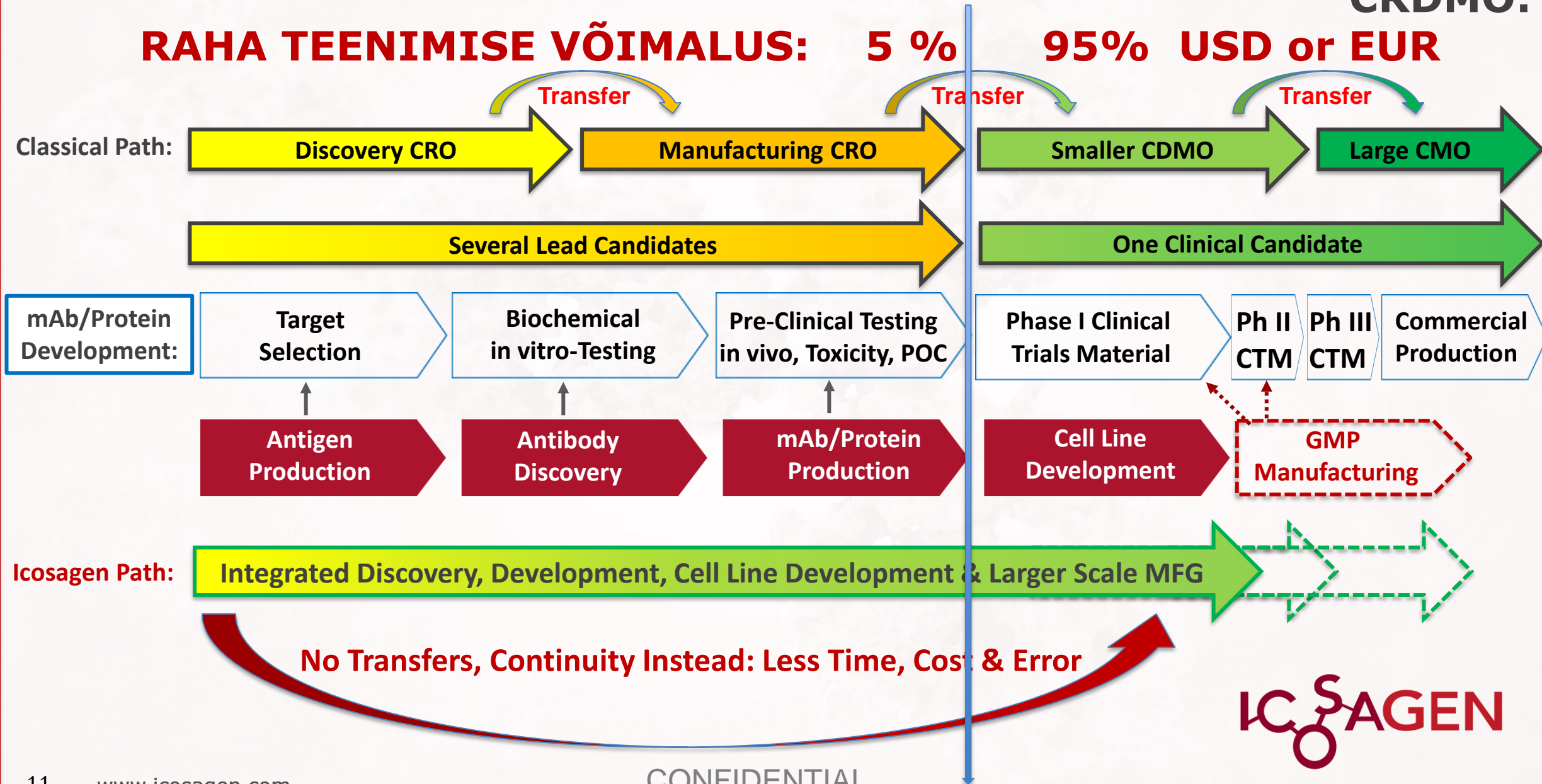
Organogram of Icosagen Group



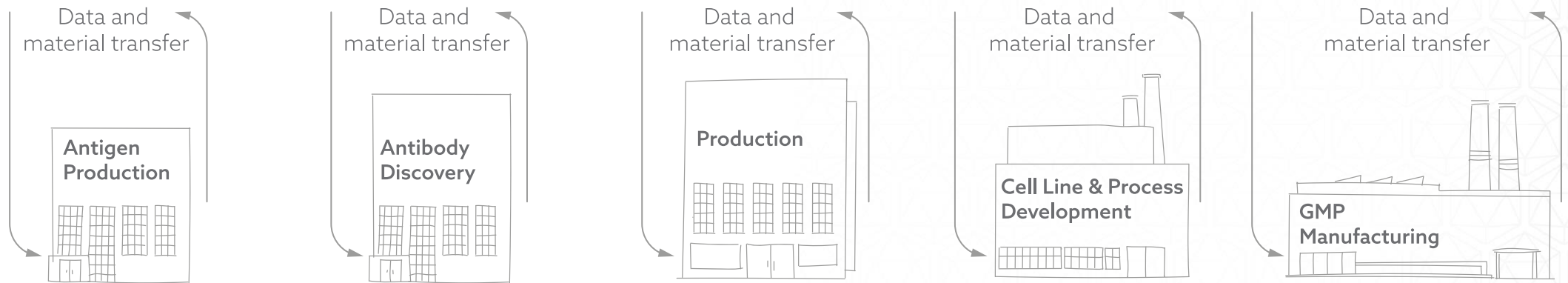
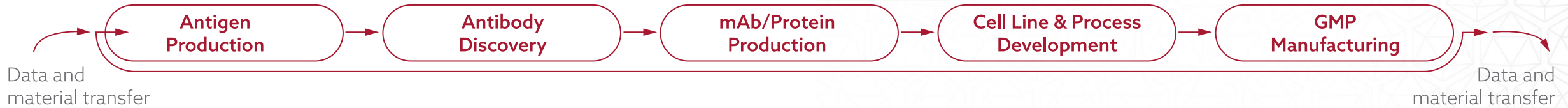
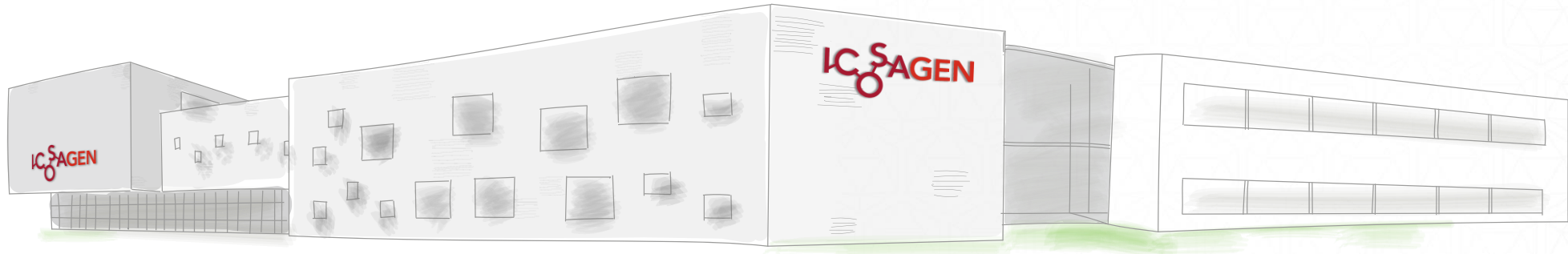
Antibodies & Proteins – Integreeritud ravimiarenduse protsess -

CRDMO:

RAHA TEENIMISE VÕIMALUS: 5 % 95% USD or EUR



The CRDMO Approach – From R&D and Pre-Clinical to Clinical Stages



In 2022, we were trusted by many partners

Partnered with

95

biotech/pharma companies

Completed

517

projects

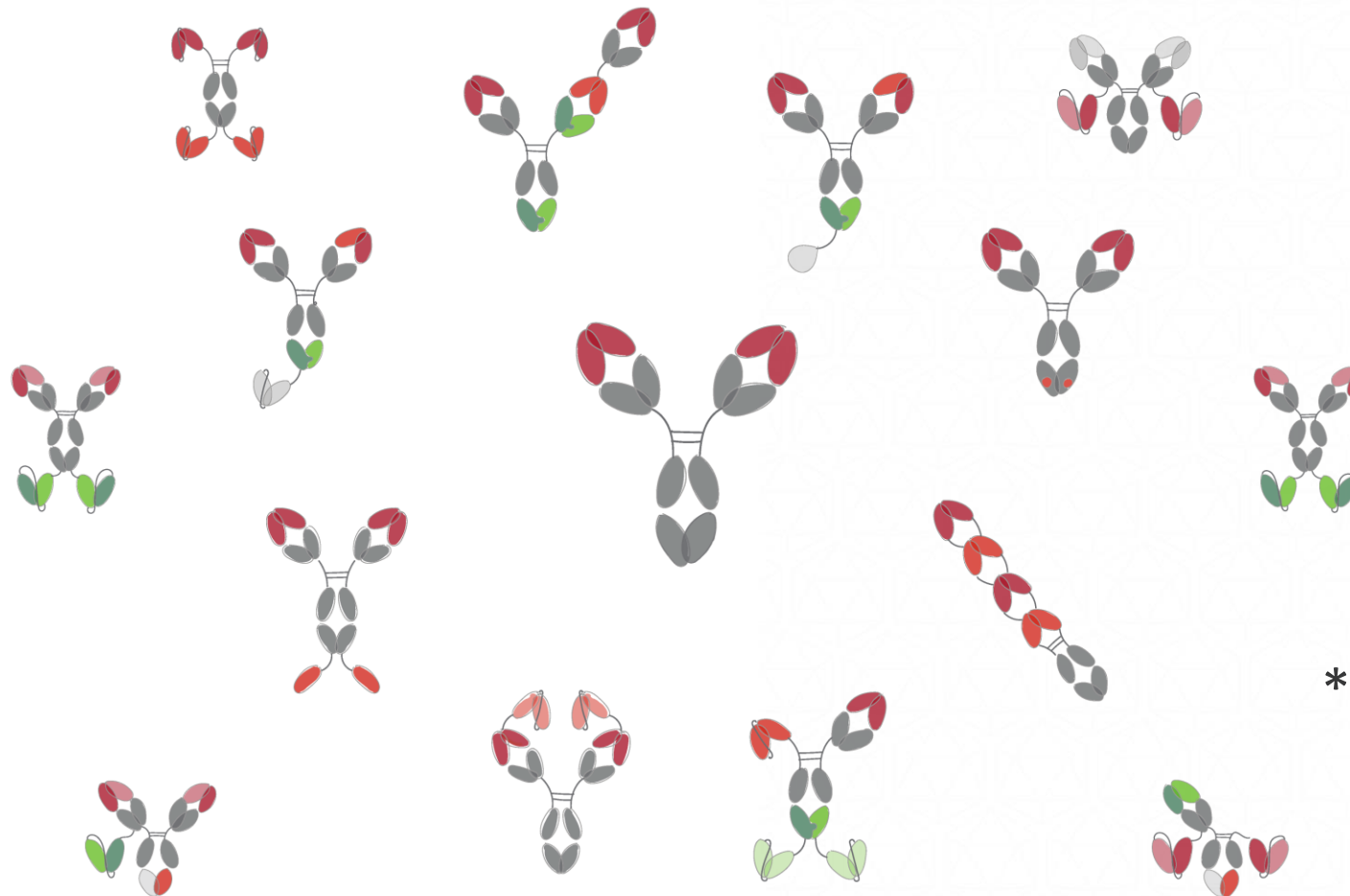
Produced

3169

different proteins

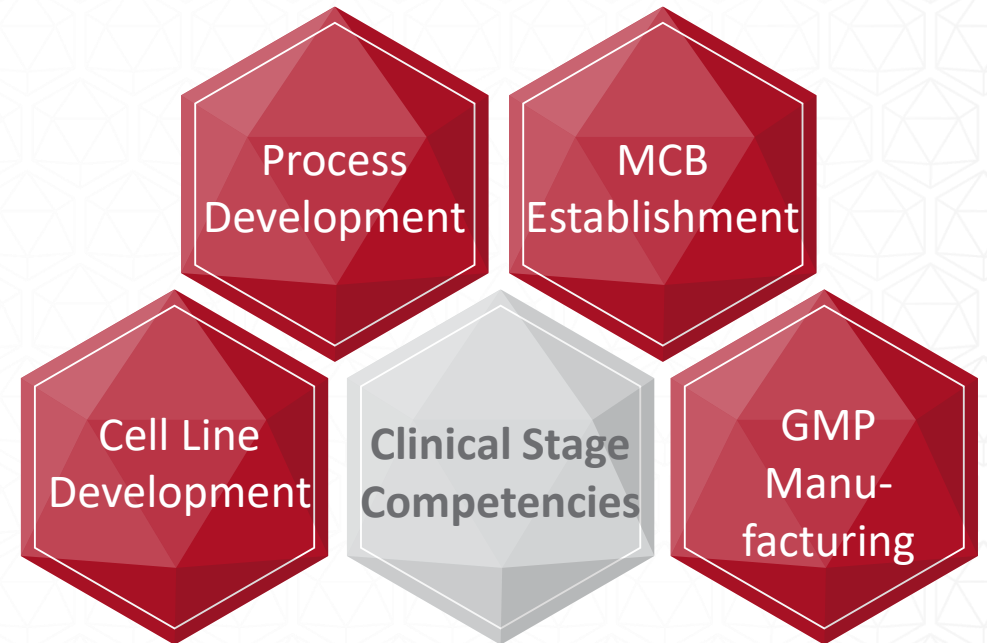
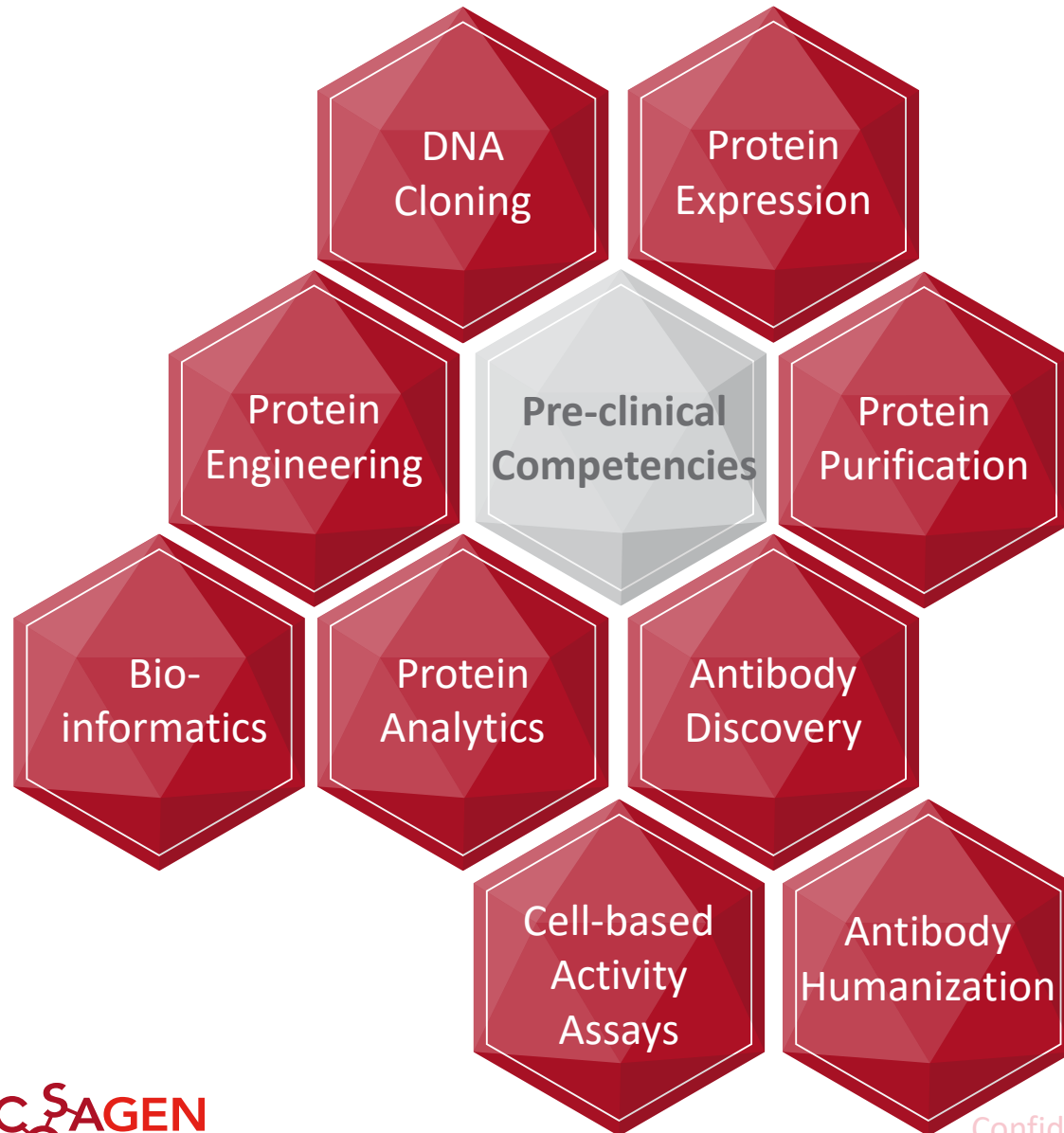
Multispecific antibodies aka Frankenbodies?

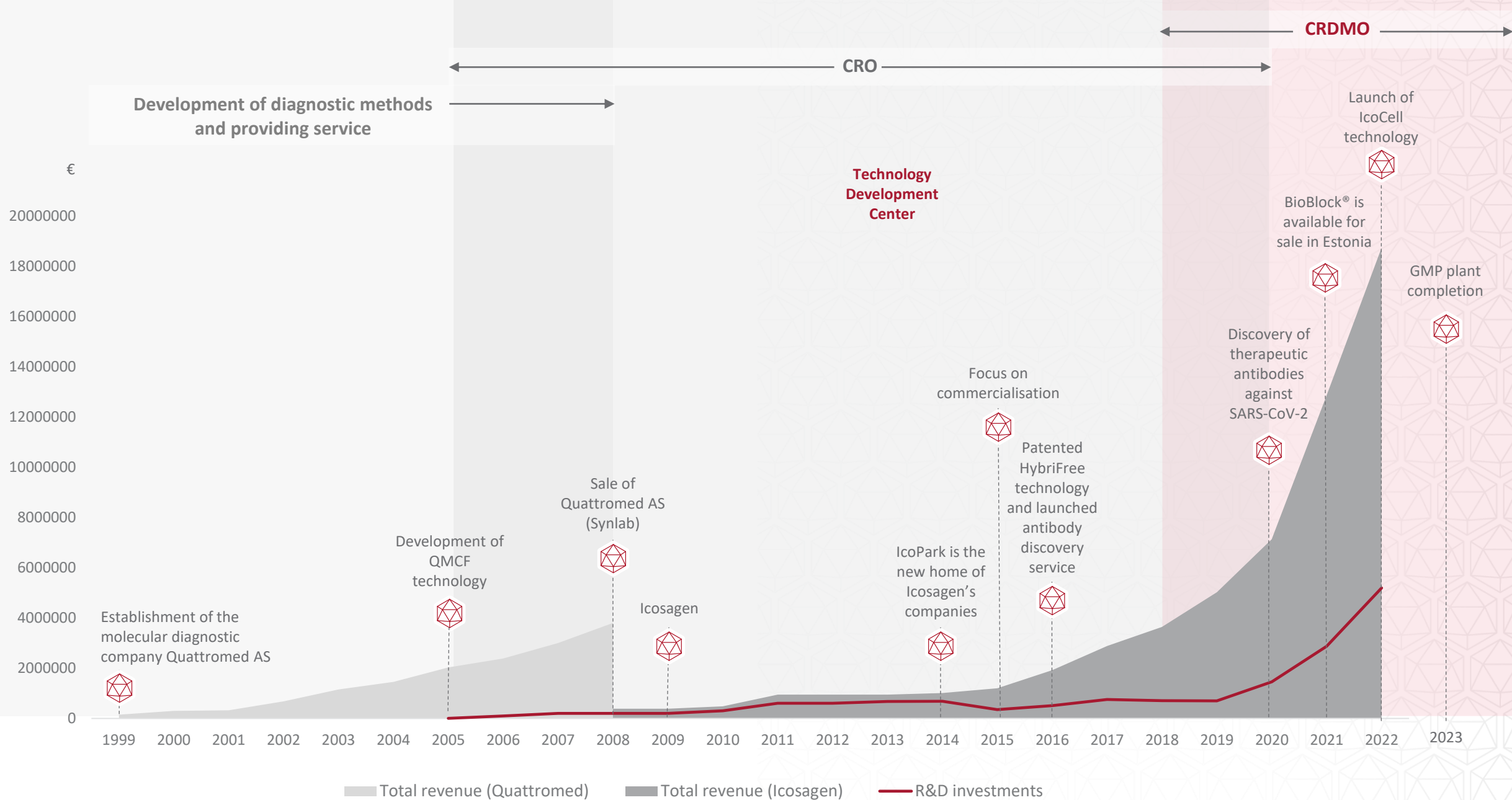
We (will) have them all produced!*



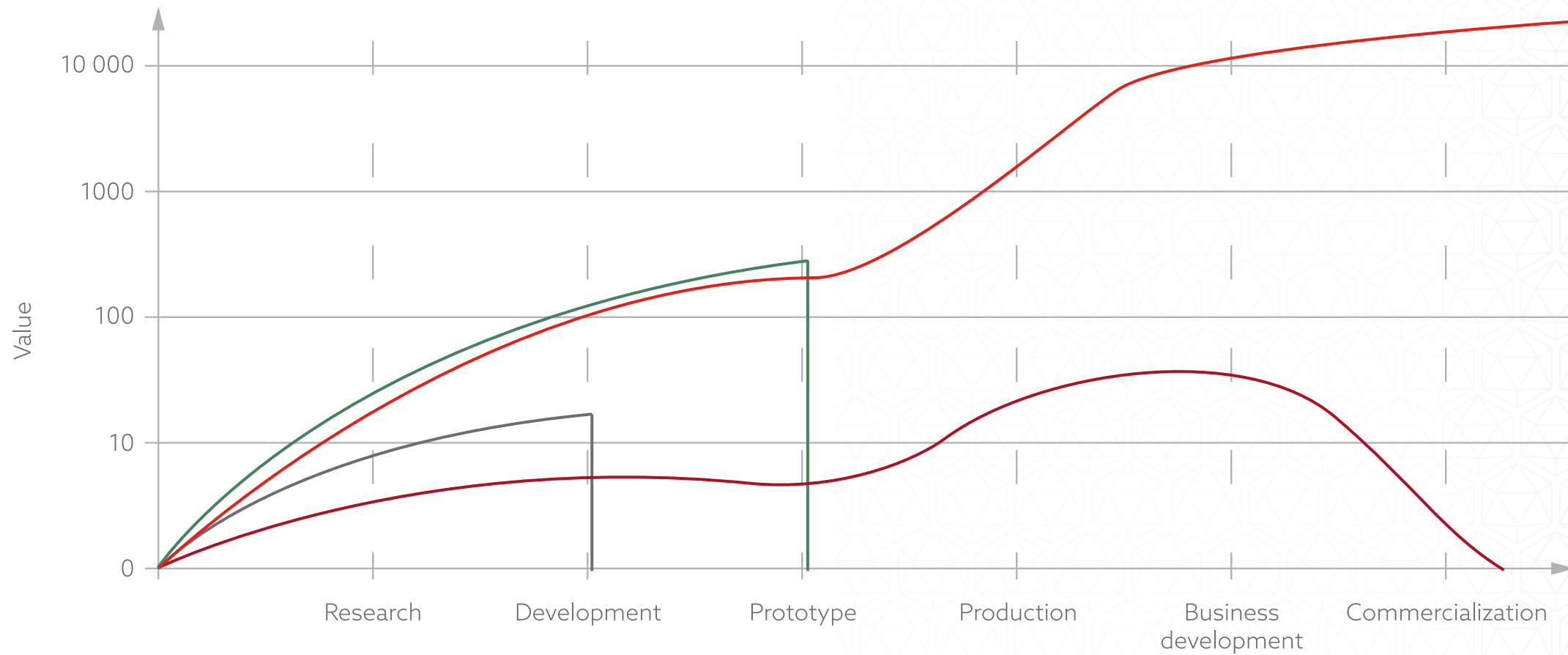
*eventually

Icosagen Core Competencies and Services

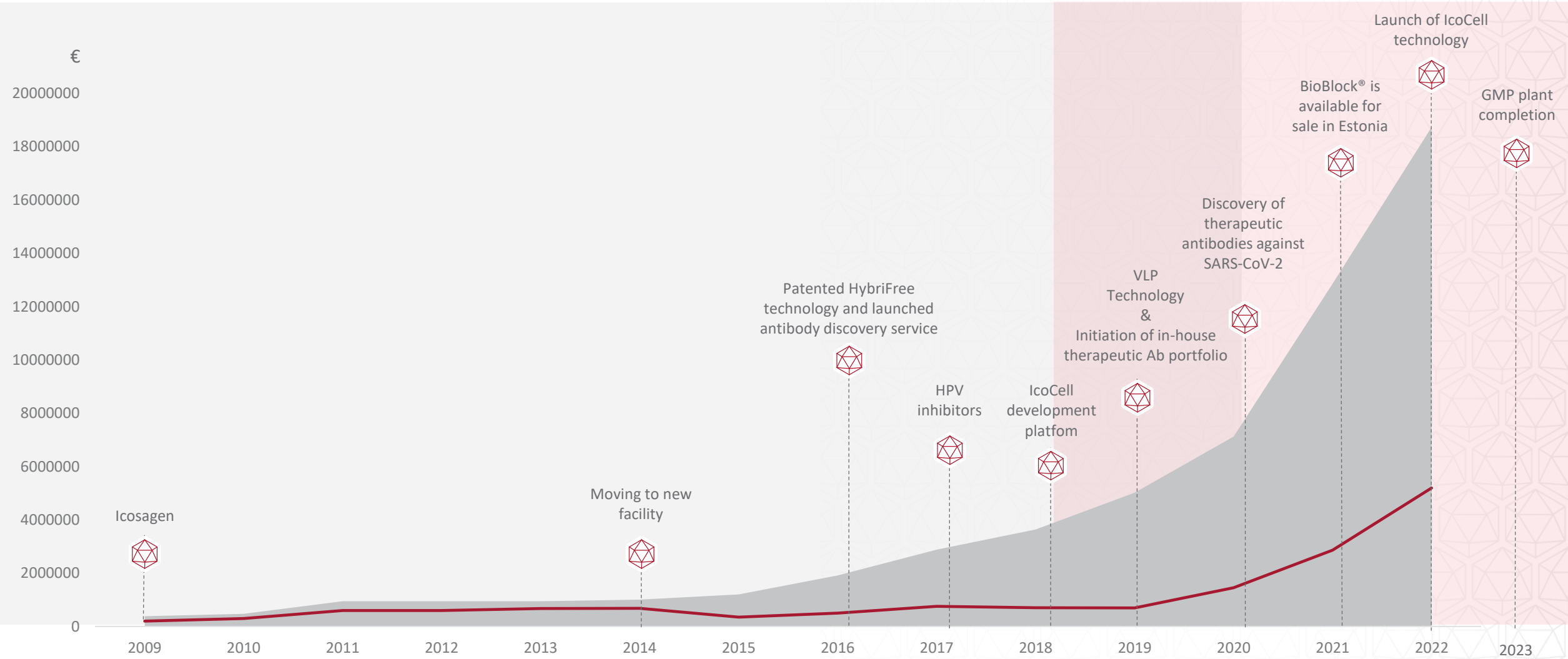




Innovation value generation arcs



Innovation projects



■ Tulud kokku — Teadus- ja arendustegevuse kulud

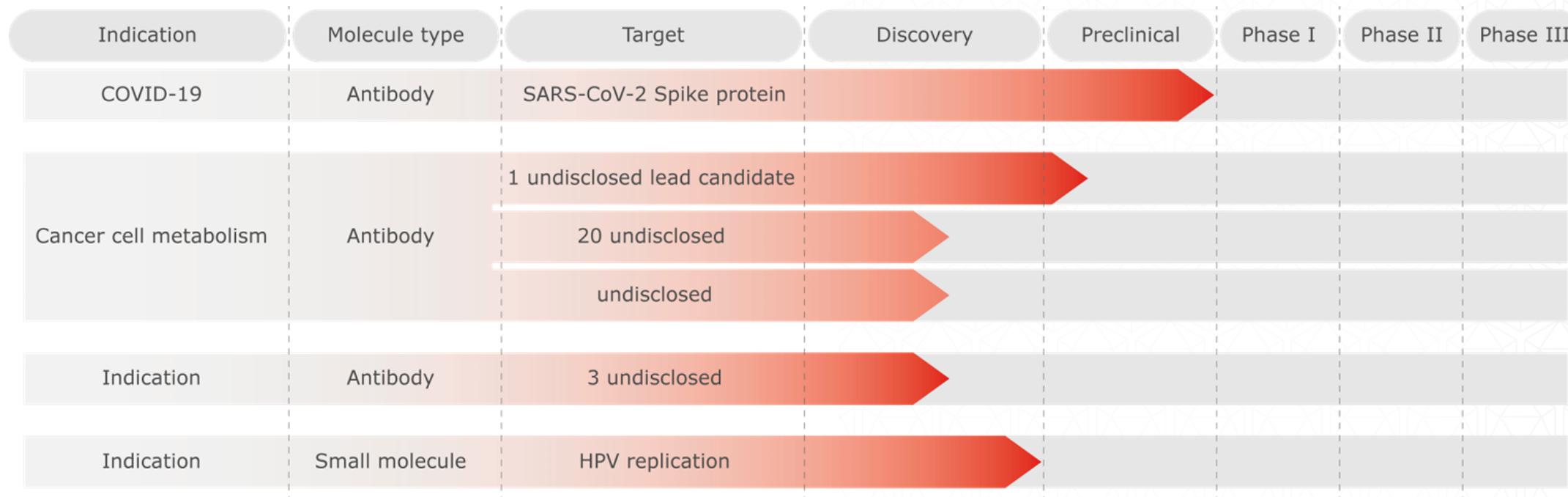


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Icosagen's vision – organic growth strategy



In-house therapeutic developments



PLOS PATHOGENS

 OPEN ACCESS  PEER-REVIEWED

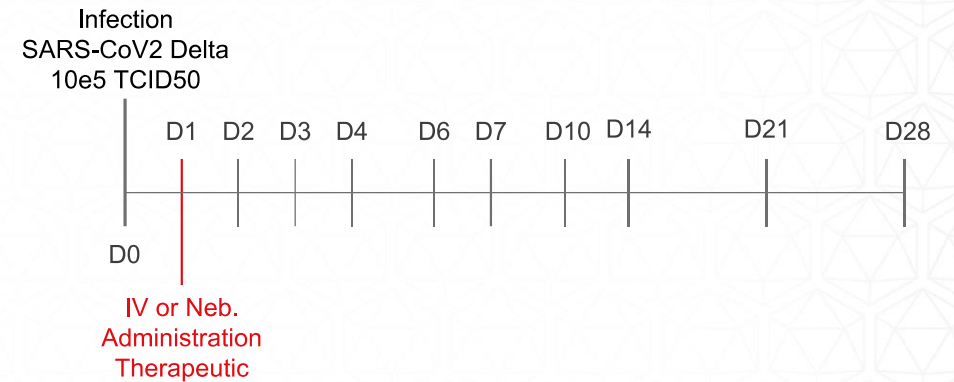
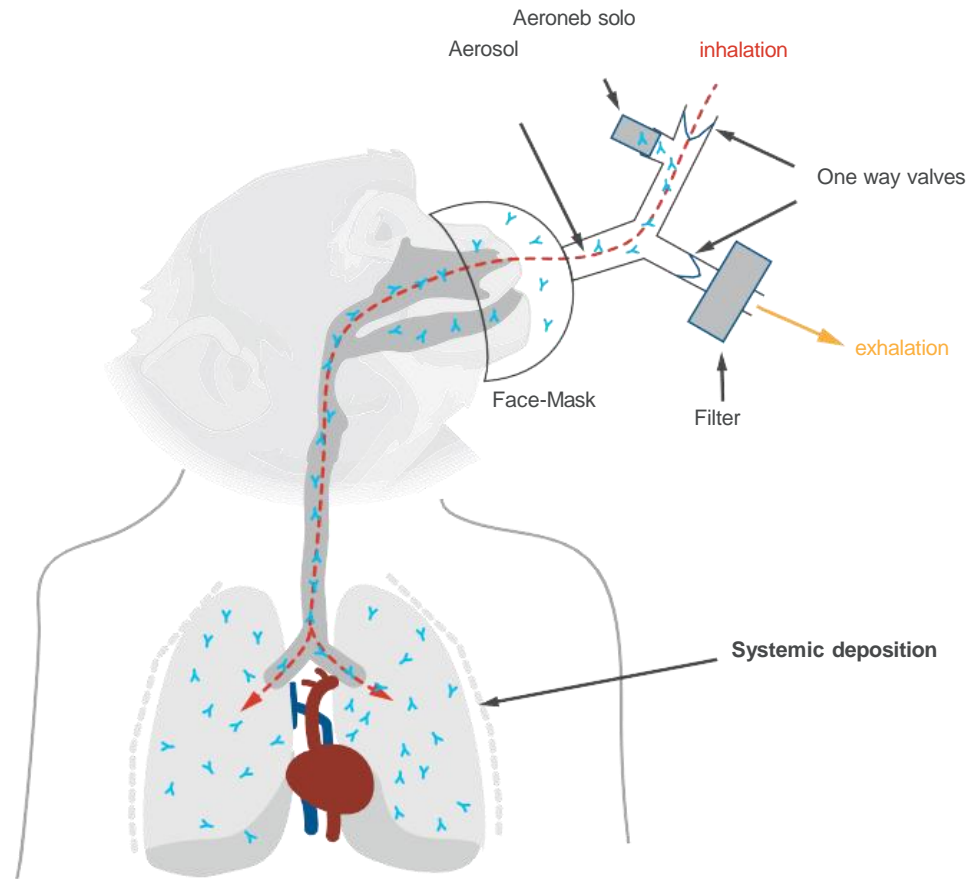
RESEARCH ARTICLE

Broadly neutralizing humanized SARS-CoV-2 antibody binds to a conserved epitope on Spike and provides antiviral protection through inhalation-based delivery in non-human primates

Paule Hermet, Benoît Delache, Cecile Herate, Esther Wolf, Gaily Kivi, Erkki Juronen, Karl Mumm, Eva Žusinaite, Denis Kainov, Eve Sankovski, Kai Virumäe, Anu Planken, Andres Merits, Jessica E. Besaw, Ai Woon Yee, Takefumi Morizumi, Kyumhyuk Kim, Anling Kuo, Asma Berriche, Nathalie Dereuddre-Bosquet, Quentin Sconosciuti, Thibaut Naninck, Francis Relouzat, Mariangela Cavarelli, Mart Ustav, Derek Wilson, Oliver P. Ernst, Andres Männik, Roger LeGrand, Mart Ustav Jr.  [view less]

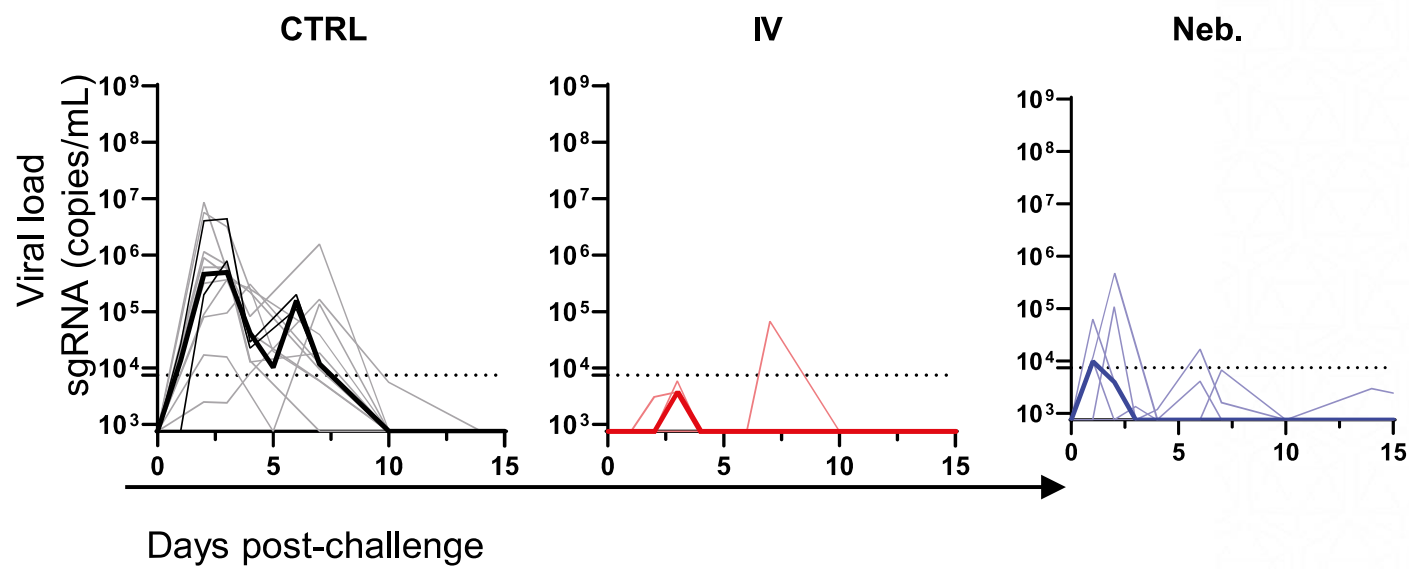
Published: August 2, 2023 • <https://doi.org/10.1371/journal.ppat.1011532>

Schematic representation of the antibody nebulization system and pharmacology study protocol

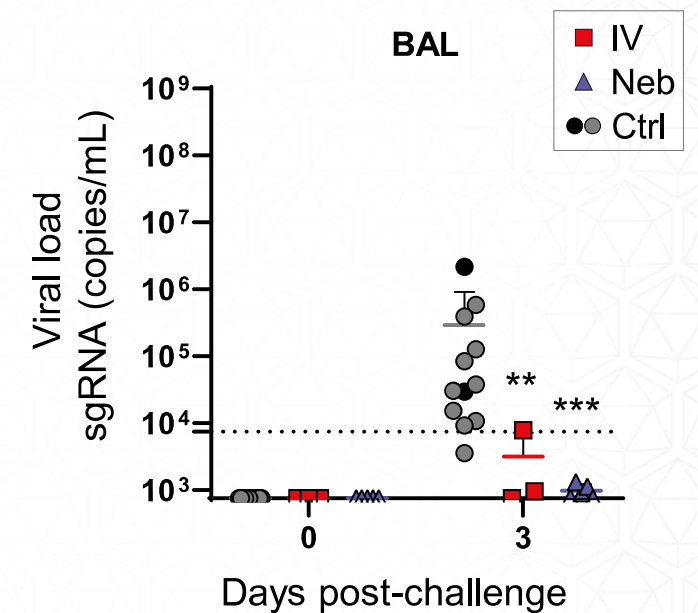


Antibody ICO-hu104 reduces viral load in non-human primates through nebulization and intravenous administration

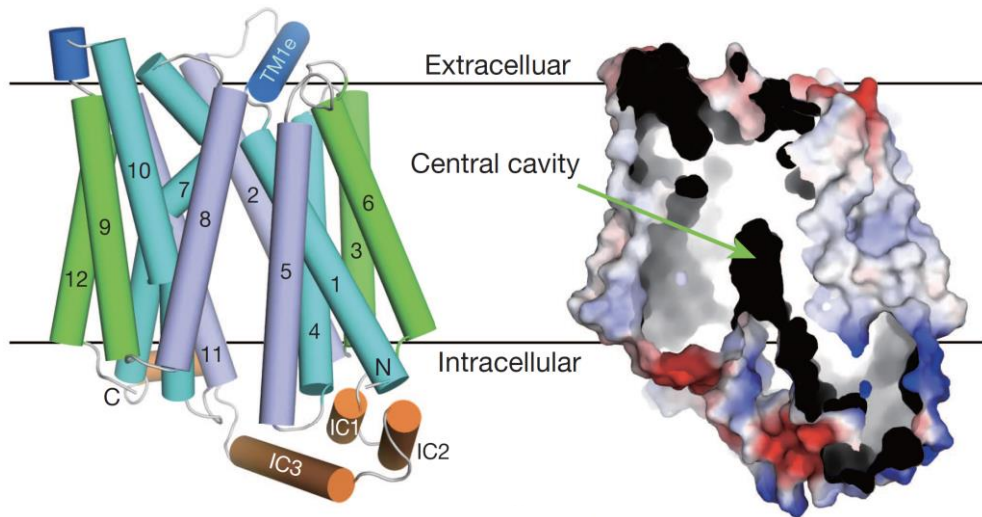
Subgenomic (sg)RNA determined by RT-qPCR in nasopharyngeal fluids



Viral loads determined by RT-qPCR of bronchoalveolar lavages (BAL)



SLC2A1 (GLUT1) – overexpressed in several cancers, predicts poor survival



- GLUT1 – 12TM glucose transporter
- Overexpressed in multiple cancers
- Small molecule inhibitors have shown preclinical efficacy
- Small therapeutic window – on target toxicity effects (seizures, mobility impairment, body temperature loss)

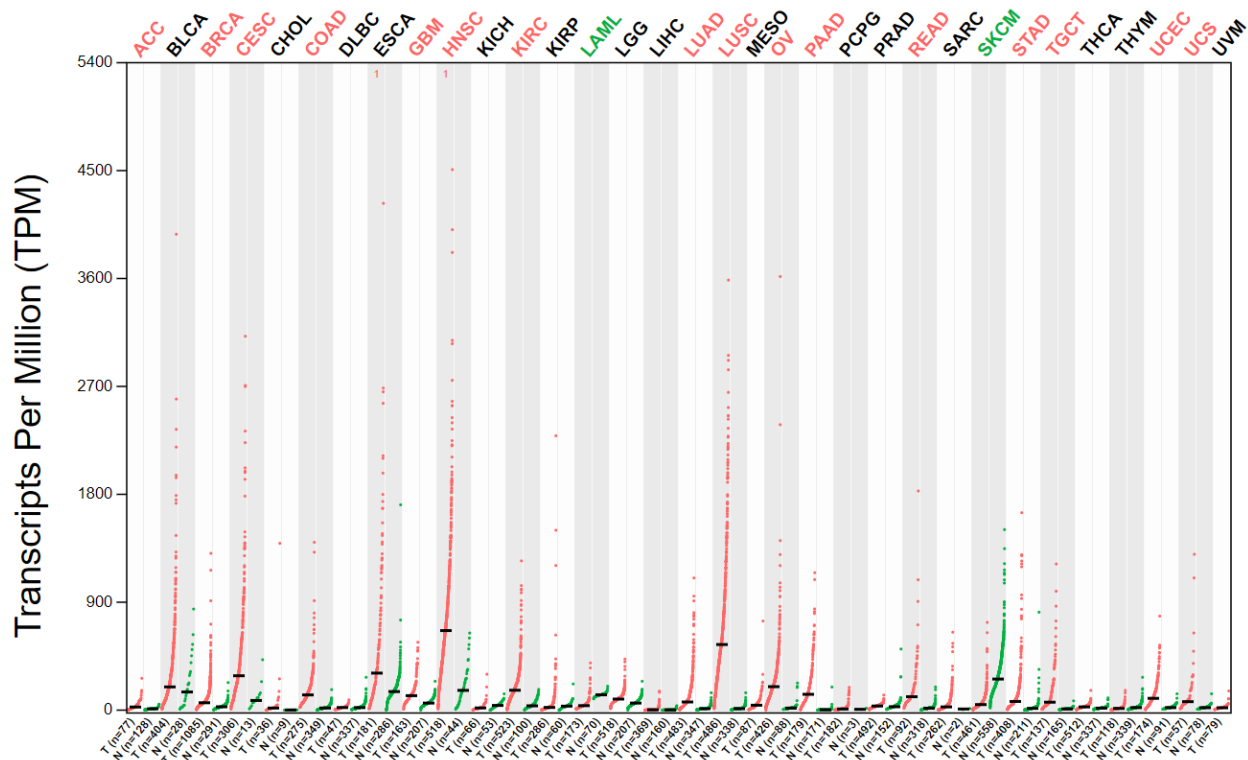
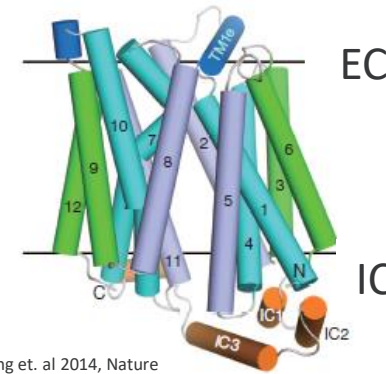
DESIGN OBJECTIVE

Highly specific inhibitor of GLUT1

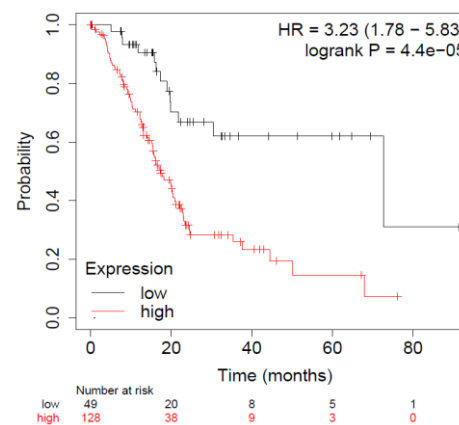
Evaluate effects as combination therapy with approved or clinically evaluated small molecule drugs

Confirm increased therapeutic window – non or limited toxicity effects in vivo

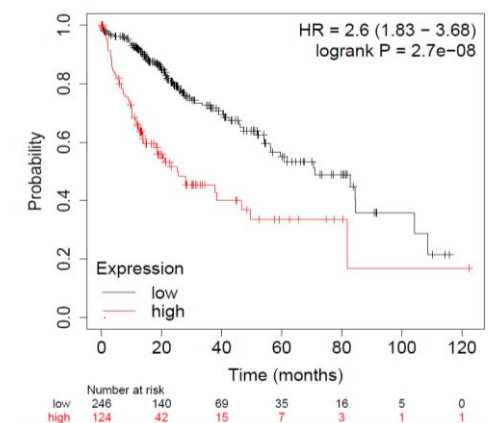
GLUT-1 is overexpressed in cancer and high expression predicts poor survival



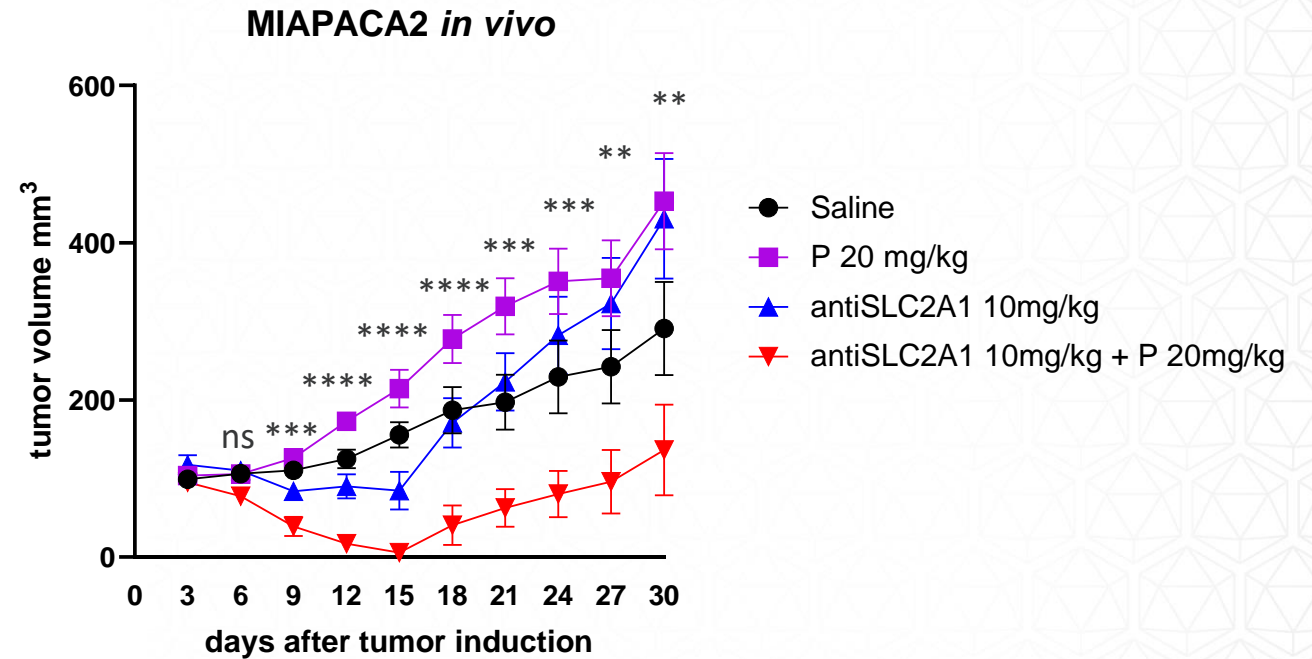
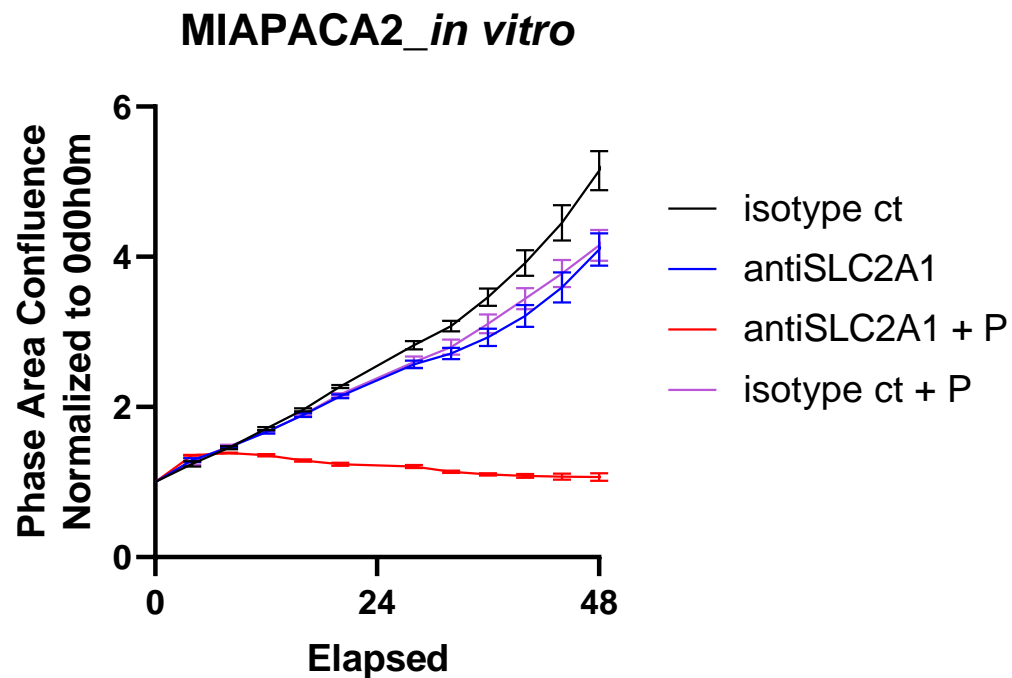
Pancreatic ductal adenocarcinoma



Liver hepatocellular carcinoma



Anti-SLC2A1 and OXPBOS Inhibitor Synergistic Tumor Growth Inhibition in vivo



Significance is shown for Phenformin vs #33 + Phenformin

In-house diagnostic developments

NEUROBIOLOGY

- CDNF
- MANF
- Artemin
- GDNF
- NGF
- BDNF
- Neurturin
- GFRA-1
- GFRA-2
- GFRA-3
- GFRA-4
- RET

METABOLIC DISEASES

- CHI3L1
- PAI1
- FGF21
- RBP4
- IGFBP1
- TIMP1 | Coming soon!
- LEPTIN | Coming soon!
- MMP9 | Coming soon!
- SHBG | Coming soon!
- Adiponectin | Coming soon!

INFECTIOUS DISEASES

- Zaire Ebolavirus GP
- MLV p30
- BPV
- HCV
- HIV-1
- HPV
- SIV1-Nef
- SARS-CoV-2 Spike
- SARS-CoV-2 Nucleocapsid
- Influenza A
- Influenza B
- SARS-CoV-2 beta variant

ISOTYPE CONTROL

- Anti-HEL isotype control

CARDIOVASCULAR DISEASES

- cTnI
- D-Dimer
- Gal-3
- CRP
- Myoglobin
- sST2
- FABP3
- cTnT
- pro-BNP | Coming soon!
- MPO | Coming soon!

KIDNEY DISEASES

- KIM1
- CysC
- NGAL | Coming soon!

INFLAMMATION

- IL-6
- PCT
- GDF-15
- Human CCL20
- Human S100-A8 and A9
- IL-33 | Coming soon!

SECONDARY ANTIBODIES

- Goat anti-mouse IgG

LATEX ALLERGENS

- Heb b1
- Hev b3
- Hev b5
- Hev b6.02

MISCELLANEOUS

- CD48, human
- CD48, mouse
- 2B4, human
- 2B4, mouse
- His-6 tag
- Elafin
- Human laminin a4 and a5
- RNase7 and 8
- Dnase I

Our mission is to establish a world-class drug development and production company in **Estonia** and provide employment for **highly qualified individuals** in Estonia.

Driving force: un-met medical needs in therapeutics and diagnostics

Development of antibody based therapeutic candidates

Providing world-class services in the development and manufacturing of biotherapeutics

Scientific excellence

Novel technologies to support product and service development

Highly professional and qualified team



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Research partners





Many thanks to our young and ambitious team members at Icosagen who are very creative and hard-working! They will make a difference and would change the World!

Also, thank you for listening!

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