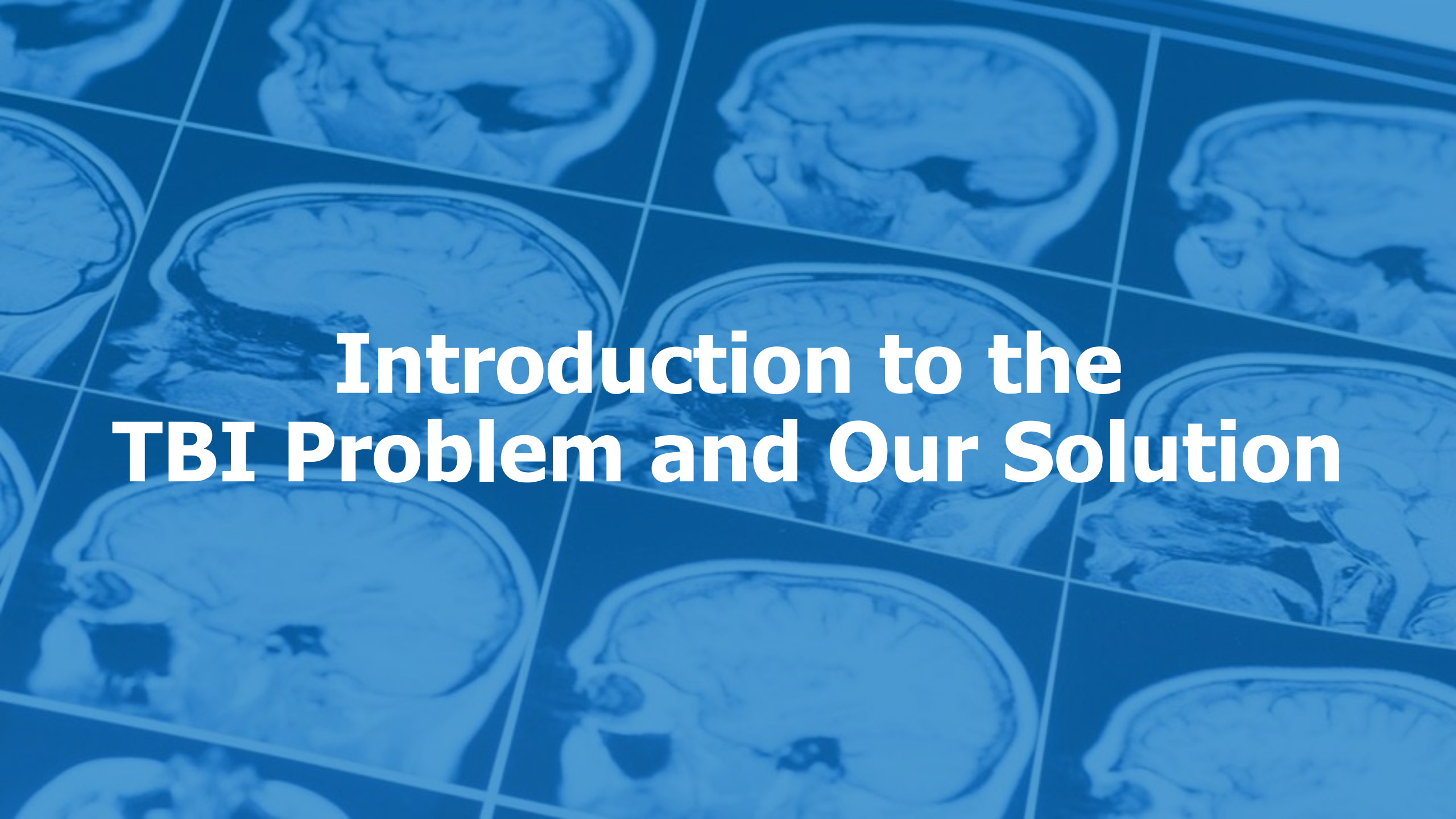
Traumatic Brain Injury

Complex problem – Creative solution

April 2025

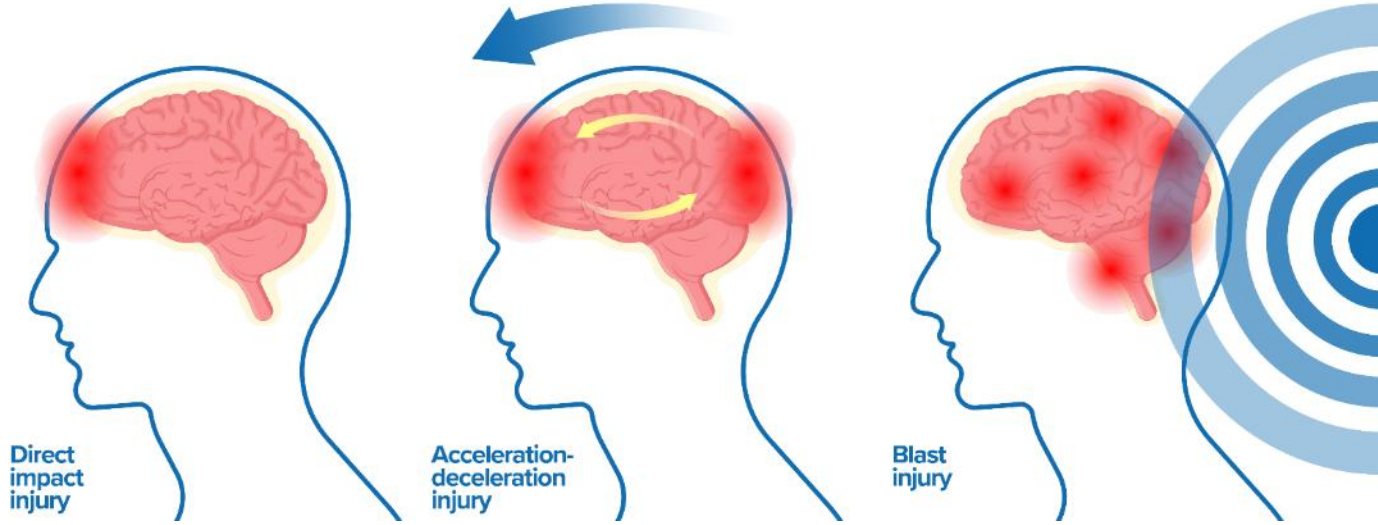
Confidential



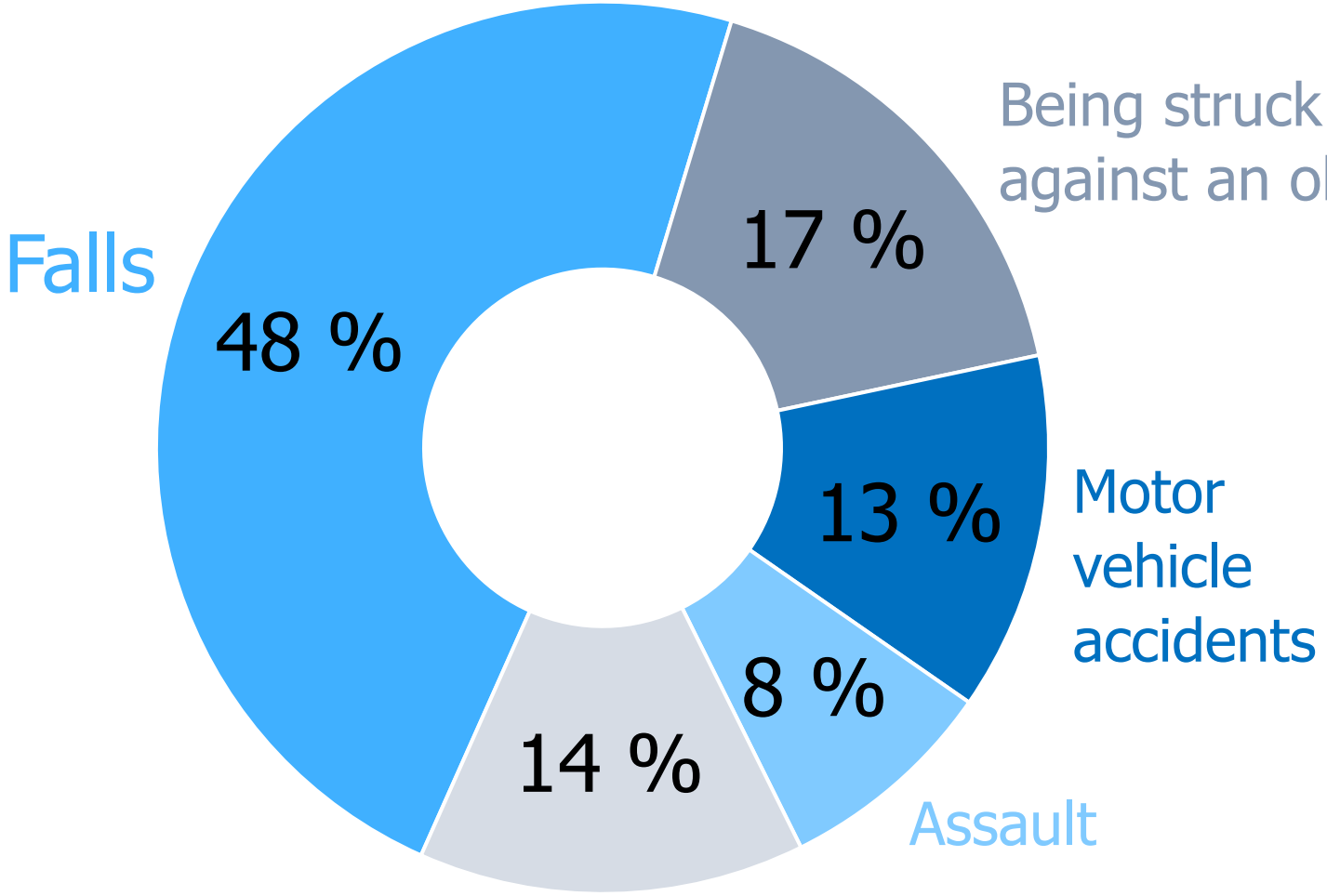
Introduction to the TBI Problem and Our Solution

Traumatic Brain Injury (TBI)

- TBI occurs after a hit to the head
  - For example, in falls, vehicular accidents, contact sports, and blasts
- It causes immediate physical damage to brain tissue
- However, it also exposes the healthy part of the brain to metal ions, free radicals and inflammation
  - Sets off a cascade of chemical reactions that damages surrounding healthy tissue
- Severe – moderate – mild TBI



Leading Causes of TBI



E.g. blasts and explosions, firearms, medical procedures

Reference: U.S. CDC

TBI – A Global Problem

New cases each year

- Around 69 million TBI cases globally *
  - 2.8 million in the US **
  - 2.5 million in Europe ***

- Most cases are closed head injuries
  - Difficult to detect, potentially risky situation
  - ~90% of cases are categorized as “mild TBI”

* Dewan et al. (2019) J Neurosurg 130: 1080-1097
** Centers for Disease Control and Prevention (CDC)
*** CENTER-TBI EU

Limitations of Current Diagnostics

- Neurological examination:
  Glasgow Coma Score (3 - 15)
  - Vulnerable to confusion, paralysis, intubation, intoxication
- Computer tomography (CT) and Magnetic resonance imaging (MRI)
  - Require hospital environment
  - Expensive procedures
  - Exposure to irradiation (CT)
  - Potential anaesthesia/sedation, especially for children
  - <u>Cannot detect mild injuries</u>

Biomarker-based Tests

- FDA-approved blood protein tests
  - Require hospital environment, equipment etc.
  - Invasive
- Medicortex is developing a non-invasive, point-of-injury test based on saliva or urine samples
- Our biomarkers are *glycans* – carbohydrate structures
  - Degradation products released to the circulation after the brain cell damage

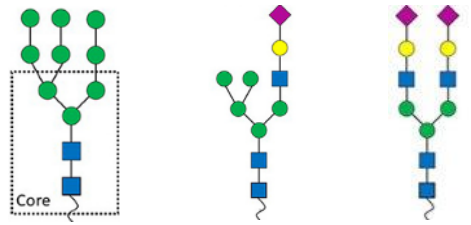
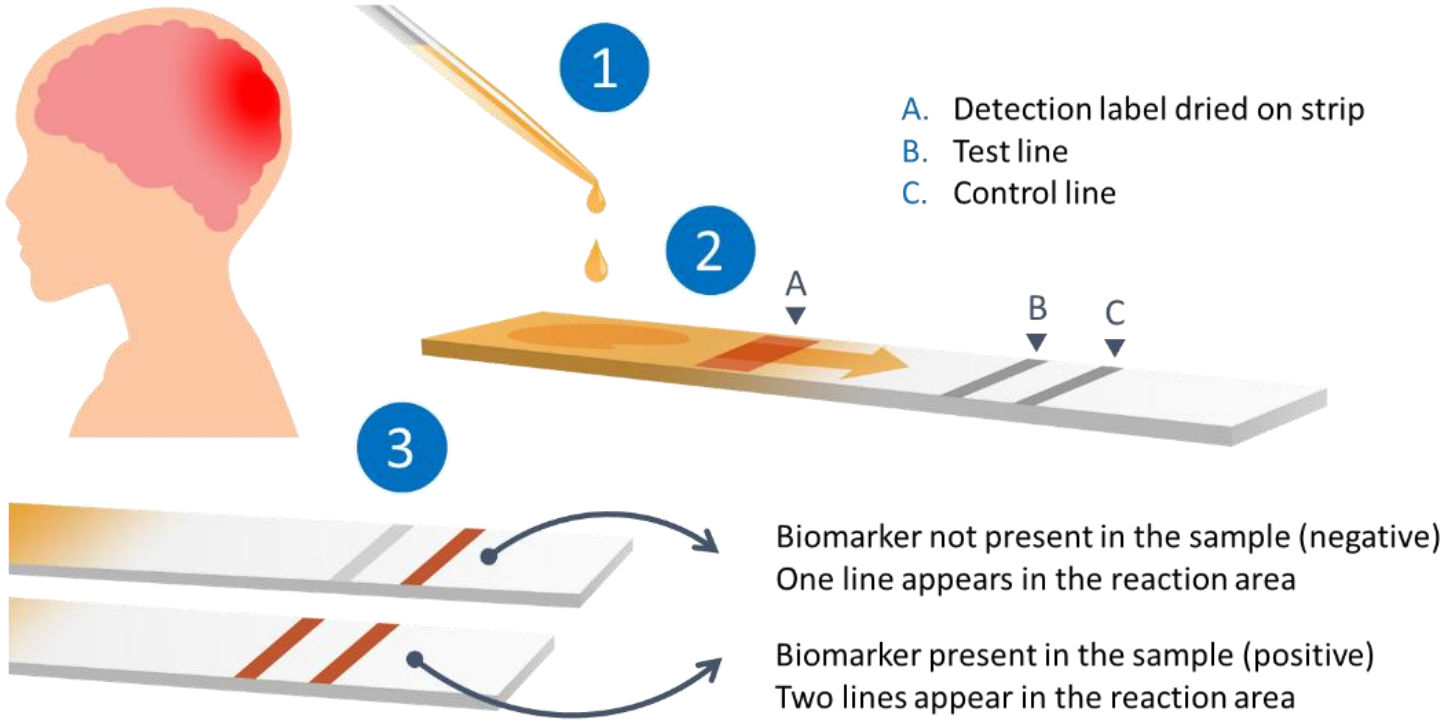


Illustration. Different glycan structures.

Our Solution for Diagnostics

1. A **urine** (ProbTBI™) or **saliva** (IndicateTBI) sample is applied on a test strip
2. The sample migrates along the strip
3. The result is readable on the strip



Research and Development: Performed and Planned

Three Clinical Studies – Published Results

1st Clinical trial: Proof-of-Concept

	Patients
Patients with suspected TBI	12
Healthy controls	12

Results published:

Kvist M, Välimaa L, Harel A, et al. (2021) Glycans as Potential Diagnostic Markers of Traumatic Brain Injury. *Brain Sciences* **11**:1480. https://doi.org/10.3390/brainsci11111480

2nd Clinical trial: TBI vs. Healthy & Orthopedic trauma

Patients with suspected TBI	24
Patients with orthopedic injury	16
Healthy controls	29

Glycan Profiling in Saliva and Urine: Exploring Potential Biomarkers for Mild Traumatic Brain Injury.
Manuscript being finalized

3rd Clinical trial: Children

Children with suspected TBI	28
Healthy control children	30

Results published:

Kvist M, Välimaa L, Harel A, Malmi S & Tuomisto A (2023) Glycans as Potential Diagnostic Markers of Traumatic Brain Injury in Children. *Diagnostics* **13**:2181. https://doi.org/10.3390/diagnostics13132181

Clinical Trials – Conclusions

- Biomarkers showed **statistically significant** differences between injured and healthy subjects – correspondence with prior animal data results
- Biomarkers were recognized by their ability to bind to several lectins
- Individual glycan profiling by mass spectrometry revealed several structures that were different between injured and healthy subjects
- Medicortex reached a significant milestone -> **a proof-of-concept**

Analysis of the samples collected in the second clinical trial was enabled by a grant received from the US Department of Defense (DoD) / U.S. Army Medical Research and Materiel Command.

Analysis of the samples from the third clinical study was supported by Business Finland.

Biomarker Detection on a Strip

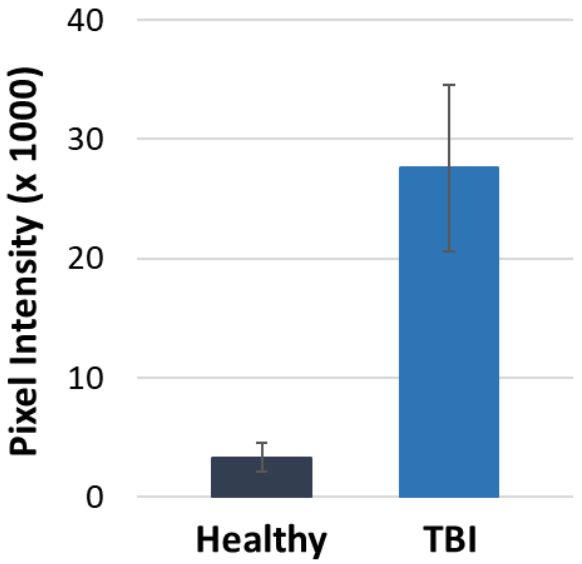
Demonstration of biomarker detection on a nitrocellulose strip using colloidal gold label

Saliva samples

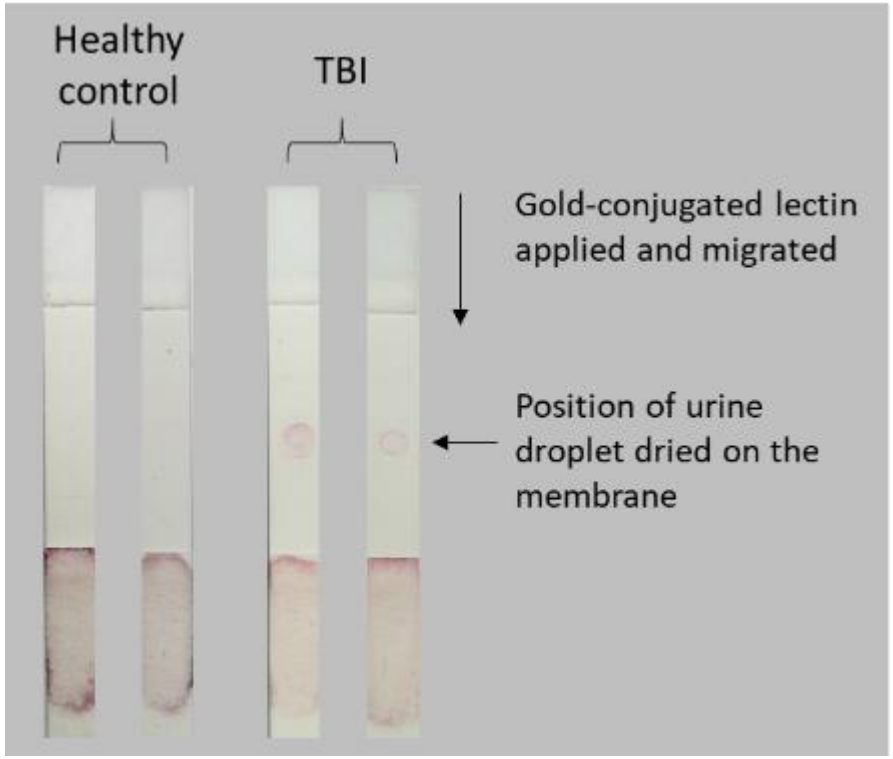
Visual outlook

Healthy **TBI**

Measured darkness of spots

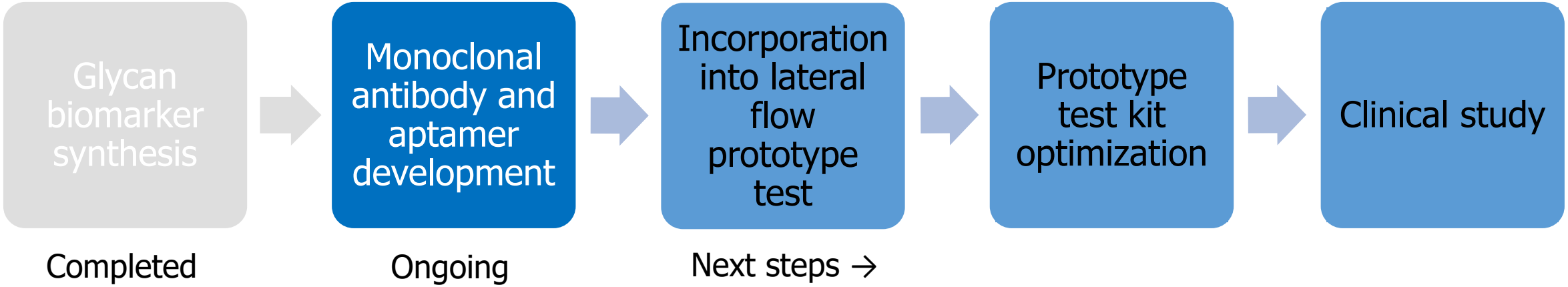


Urine samples



Biomarker Synthesis and Binder Development

- Medicortex has resolved the structure of the biomarker and produced an equivalent synthetic structure for binder generation and assay development
- Monoclonal antibodies and aptamers (among other binders) are currently developed as binders of the biomarker



R&D Plan for Saliva/Urine Test Development

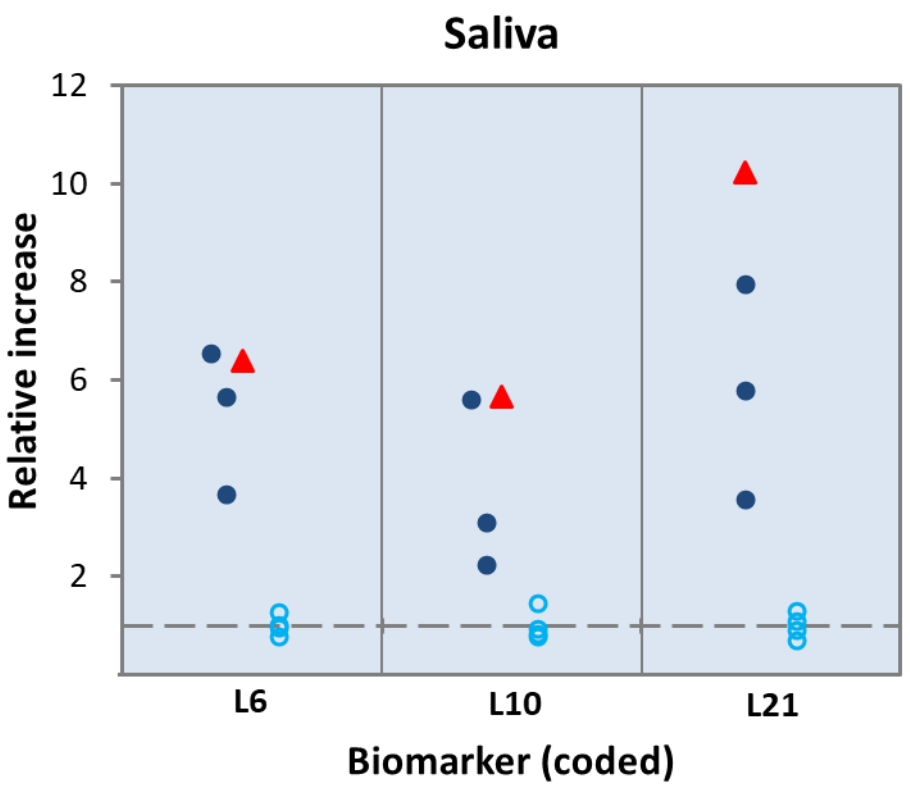
	2025/Q1	2025/Q2	2025/Q3	2025/Q4	2026/Q1	2026/Q2	2026/Q3	2026/Q4
Binder development								
Prototype kit assembly								
Evaluation of the prototype								
Initiation of regulatory process								
Production of prototype batch								
Clinical evaluation of the final product								
New patent applications								

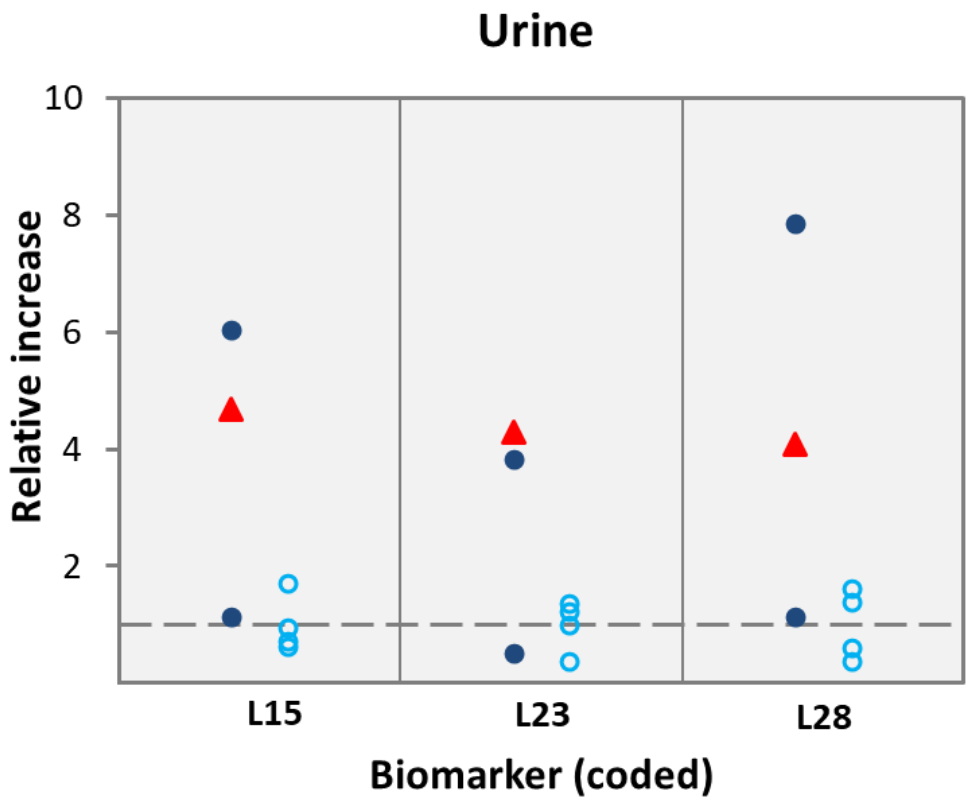
Case Study – Testimonial

- It´s winter in Turku, Finland
- A person is jogging, slips on the icy sidewalk and hits his head, losing consciousness for a few minutes
- Magnetic Resonance Imaging (MRI) is performed immediately after the injury at the local hospital
  - No clinical observations of recent brain injury were found
  - The "healthy" patient was sent home
- Medicortex performs biomarker analysis on patient's urine and saliva
  - High levels of biomarkers are detected, similar to those of confirmed TBI-patients (see next slide)

Case Study – Biomarker results

Example on three biomarker levels in saliva and urine; relative increase over the average healthy level





▲ Suspected TBI-case ● Confirmed TBI-patients ○ Healthy Controls

Case Study – Second MRI

MRI scanning was repeated after the biomarker results

- MRI showed frontal cranial hemorrhage and minor blood degradation products that were not detected in the first MRI
- Radiologist stated that alterations may be related to the recent head injury

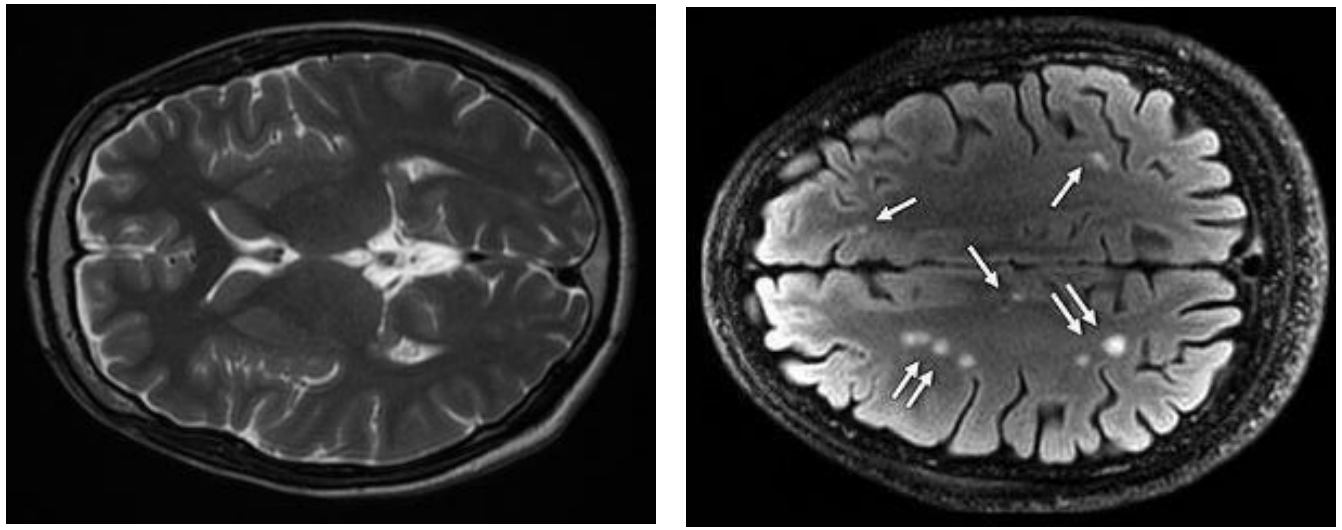


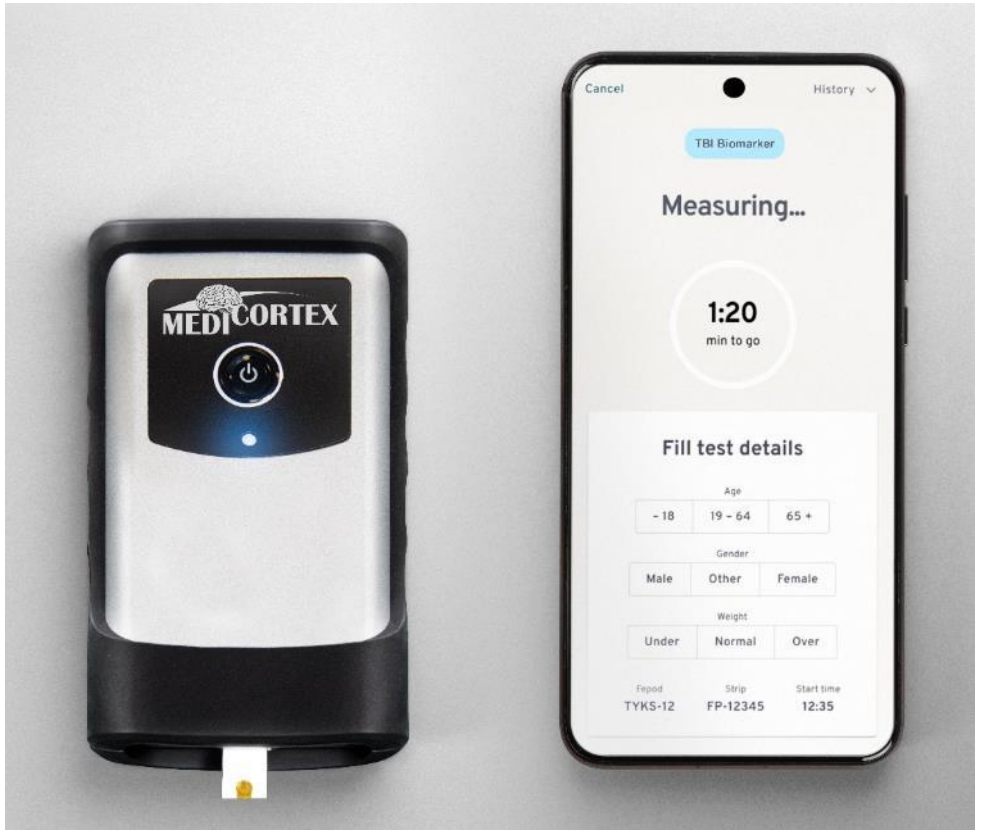
Illustration of MRI findings in TBI
(not from the case study)
Left – normal Right - TBI

2nd Generation Quantitative Test

MEDICORTEX
Heading Towards a Solution

Electrochemical sensor and device for quantitative measurement (TesTBI)

- Recognition of the biomarker in sample by highly specific synthetic binding molecules (aptamers)
- Biomarker in sample triggers an electric signal on sensor which is translated to quantitative value through unique software
- Collaboration with Fepod Oy Ltd (www.fepod.fi)
- Funding is searched for expanding the project



Illustration

Medicortex Test Advantages

ProbTBI™ Kit

TesTBI Reader Device

Affordable

Can be sold "off the shelf"

Fast

Mobile

Easy to use

Patient friendly

No radiation or contrast agent exposition

Reusable

Quantitative

Our Potential Clients

Army paramedics

Hospitals and emergency rooms

Paramedics

First responders

Sport teams

Schools

Nursing homes

Private people

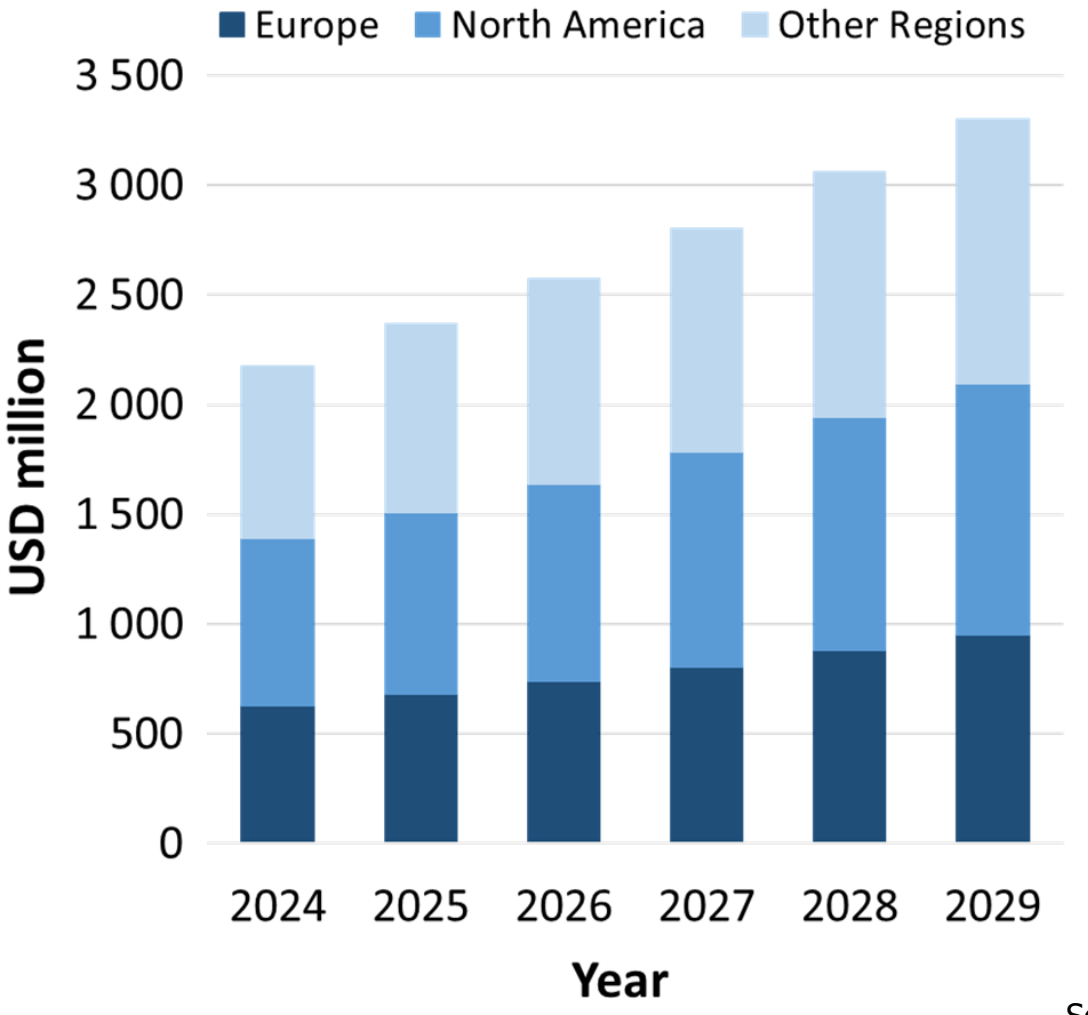
Insurance companies

Pharma companies

Medicortex is targeting **B2B institutional customers**

TBI Market

Global TBI diagnostic market expected to reach **$3.3 billion** by 2029

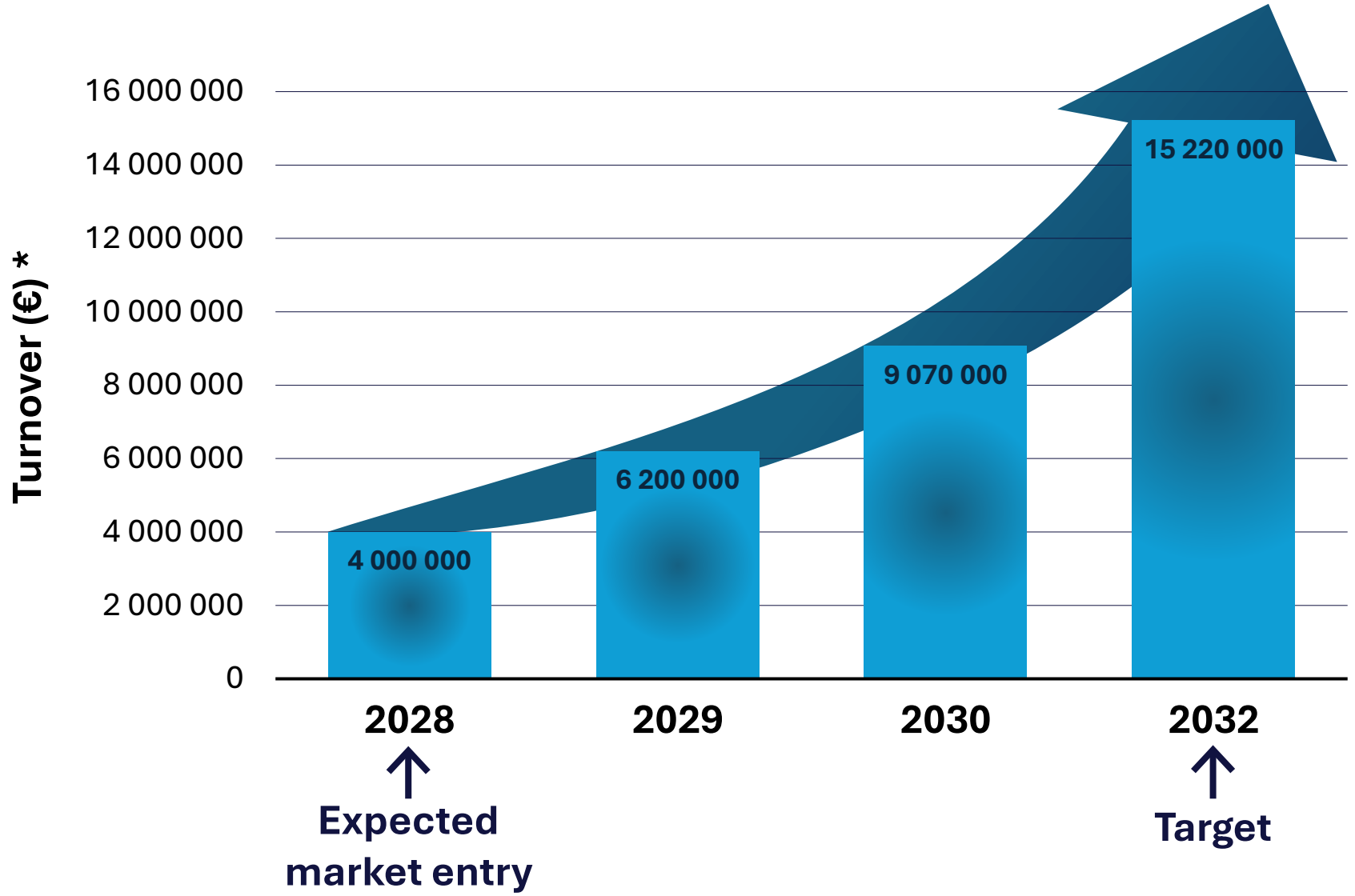


Source: Cognitive Market Research

Market growth can be related to increase in population, aging population, increased number of vehicles on the road, and extra leisure time to get engaged with risky activities, as well as enhanced clinical classification and diagnostics

* Includes sales to organizations and pharmacies as well as e-commerce sales

Sales Growth



Drug Development: Future Prospects

Neuro-protective Medication for Brain Injury

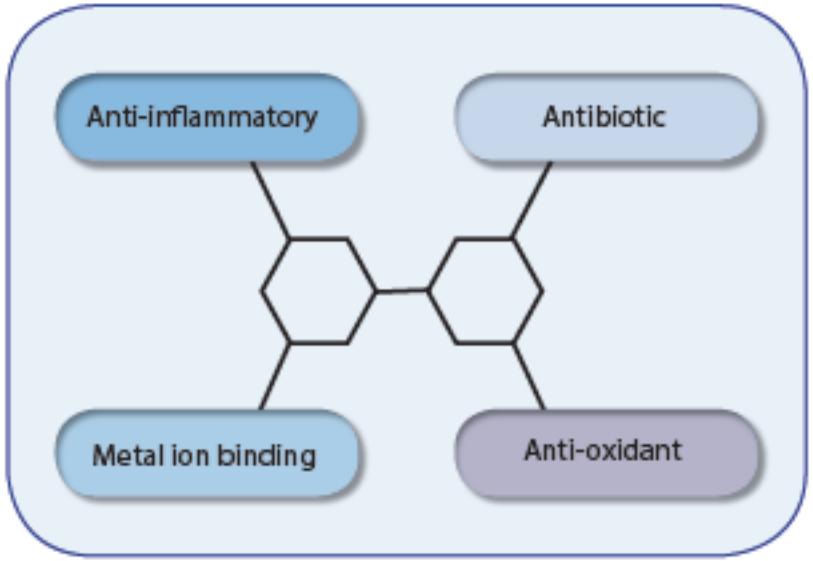
- Medicortex has designed and patented several compounds (New Chemical Entities, NCE) with multiple neuroprotective functionalities
  - Potential **drug candidates** for halting the exacerbation of the brain injury (secondary injury)
- Secondary injury involves multiple biochemical reaction cascades occurring in the brain
- A multifunctional drug is believed to have higher therapeutic potential than previously studied drug candidates which targeted single reaction pathways

Neuro-protective Medication for Brain Injury

MEDICORTEX
Heading Towards a Solution

- Two compounds (**TBI-466** and **MCF-013**) have been chemically synthesized
  - Found to be safe in preclinical escalating dose studies

- The compounds
  - Have the ability to cross the blood-brain barrier (BBB)
  - Contain a newly designed chemical spacer on which at least two functional groups are attached
  - Have several neuroprotective properties:
    - ✓ Binding of free metal ions
    - ✓ Anti-oxidation
    - ✓ Anti-inflammation
    - ✓ Free radicals scavenging



Intellectual Property Position

Patents for the Biomarker and Diagnostics

1. Prognostic and Diagnostic Glycan-based Biomarkers of Brain Damage
   - European patent No. 3283880
   - US patent No. 10,739,335
   - Canadian patent No. 2,982,503
   - Israeli patent No. 254 980
2. Non-invasive Brain Injury Diagnostic Device
   - Israeli patent No. 268,793
   - South African patent (number pending)
   - Utility model granted in China and Australia
3. Device and Method for Detecting of Brain Injury in a Subject
   - Australian innovation patent No. 2020104474
   - Finnish utility model No. 13179

Patents for the Biomarker and Diagnostics
(continues)

4. A Method for Determining a Lectin-binding Glycan Indicative to Traumatic Brain Injury
   - European patent No. 4133279
5. A Method for Diagnosis of Traumatic Brain Injury
   - Finnish patent No. 130340
   - PCT-application WO 2023/161557
6. Method of Detecting Tissue Damage
   - Finnish patent No. 130428
   - Divisional Finnish patent No. 130798
   - PCT-application WO 2023/161553
7. A Hand-held Liquid Sample Collection and Testing Device
   - Finnish utility model No. 13331
   - German utility model No. 20 2023 100 246

Patents for the Drug Development

1. Multivalent Compounds for Use in the Treatment and Prevention of Brain Damage
   - US patent No. 9,975,846
   - Finnish patent No. 127024
   - Israeli patent No. 251407
   - European patent No. 3201173
2. Conjugates and Conjugates for Use in Preventing or Treating of Brain Damage and Neurodegenerative Diseases
   - Finnish patent No. 130262

Patent for COVID-19 Diagnostics

1. Method for Determining Coronavirus and Kit for the Same
   - European patent No. 3911956

Public and Private Financing

Equity up to Now

- About 3.4 M€ from the founder and 299 private investors
- Total number of shares issued about 22.1 million
- Current price per share 1.00 € and total valuation 22.1 M€

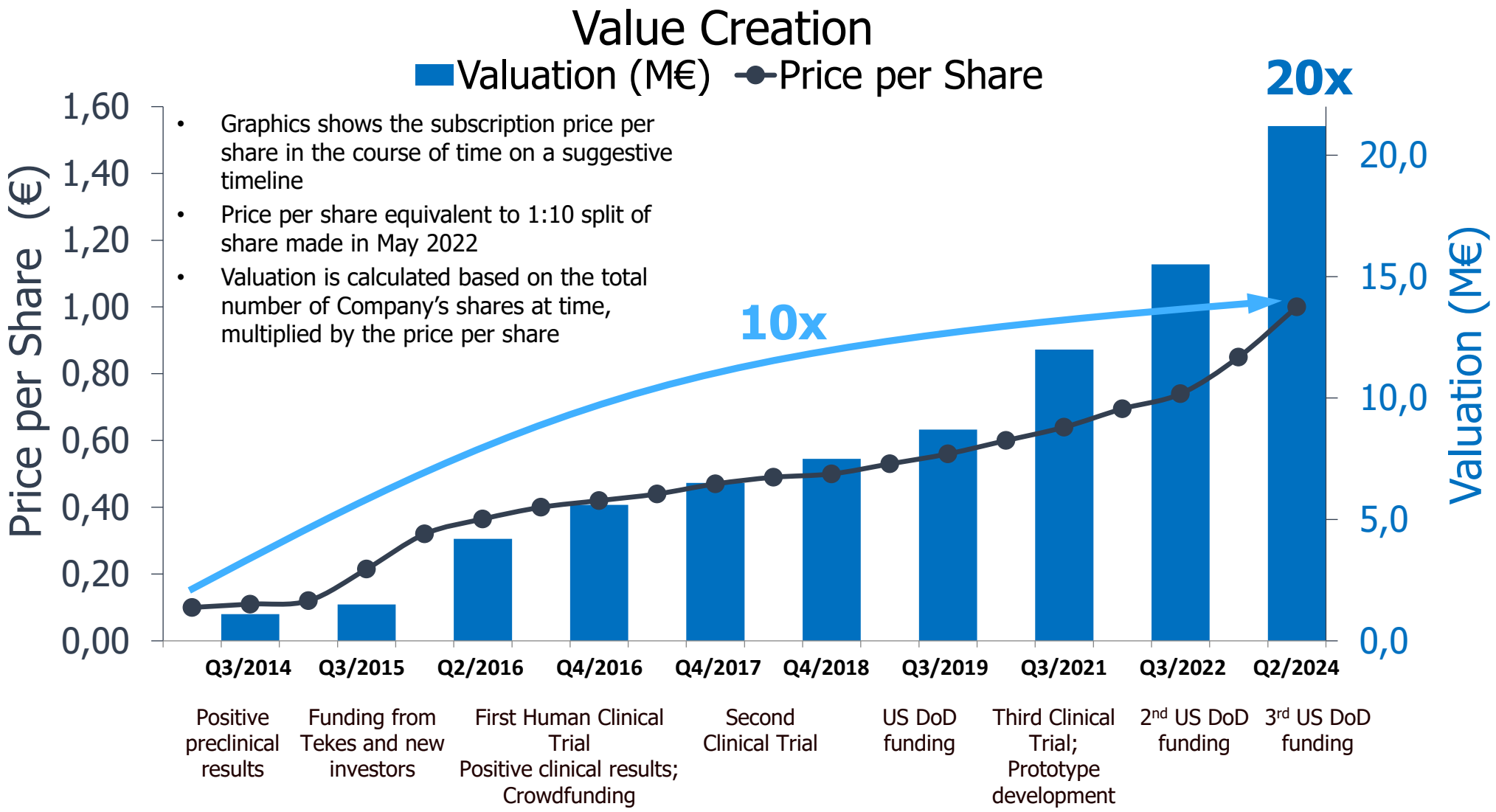
Subsidies in the Past / Ongoing

- Total of 5.2 M€ in grants
  - Including 4.6 M dollars from the US Department of Defense
- 70 k€ in awards
- **Medicortex is looking for investors:**
  - https://www.medicortex.fi/eng/investors/

Funded by the European Union

ELY Centre

From 2014–2024 Increase in Value



Use of Funds 2025-forward

New investments will be used for the diagnostic kit development:

- Further development/improvement of assay chemistry
- Saliva/urine prototype test development and assembly
- Prototype manufacturing
- Validation in clinical experiments
- Initiation of the regulatory process

Board of Directors

- Chairman of the Board - Anna Tenstam, MSc, MBA, served as a manager and board member in several companies
- Dependent Member – Adrian Harel, PhD, MBA, Founder and CEO of Medicortex
- Independent Member - Nils Grönberg, experienced Executive in many companies and foundations
- Independent Member - Ville Ranta-Panula, MSc, MBA, experienced drug development and business development professional

The Team

CEO, Founder
Adrian Harel
PhD, MBA

CSO
Lasse Välimaa
PhD

COO
Pihla Miettinen
MSc

Research Scientist
Leonardo Lara-Valderrábano
PhD

Product Manager
Begum Utz
PhD

Senior Scientist
Ivette Bañuelos
PhD

Development Engineer
Kaisa Leppä
MSc tech.

Medicortex in the Press

1. Medicortex Finland Plc signed a 1.4 million dollars research grant contract with the U.S. Department of Defense
2. Medicortex Finland Plc appointing new members for the Board of Directors
3. Medicortex was granted a European patent for detection of biomarker indicative to brain injury
4. Business Finland supporting Medicortex
5. Medicortex was granted a Finnish patent related to the detection of tissue damage
6. Medicortex Finland was granted a European patent related to the diagnostics of COVID-19 in saliva

YouTube videos

- How repeated concussions affect your brain
- Concussion in sports and Medicortex test
- Concussion in army personnel and Medicortex test

LinkedIn™ group

- The Science Behind TBI
  - Posts and discussion about science and research on TBI
  - >3,000 members

www.medicortex.fi

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