

IR Session 2023

IVD Business

Progress of R&D Activities and CDMO Business
(Neuro/Alzheimer and Ultrasensitive Detection Technology)

December 1st, 2023

Agenda

(1) Progress of IVD Business Strategy (Overview)

H.U. Group Holdings, Inc., Executive Officer (IVD)
Fujirebio Holdings, Inc., President and CEO
Goki Ishikawa

(2) R&D Activities and CDMO Business in Neuro/Alzheimer field

Fujirebio Holdings, Inc., Board Member (Neuro Business)
Fujirebio Europe NV, CEO
Christiaan De Wilde

ADx NeuroSciences, CEO
Koen Dewaele

(3) Ultrasensitive Detection Technology and CDMO Business

Fujirebio Holdings, Inc., Board Member (R&D)
Katsumi Aoyagi Ph.D.

Fluxus Inc., CEO
Peter Wagner Ph.D.

Progress of IVD Business Strategy (Overview)

H.U. Group Holdings, Inc., Executive Officer (IVD)
Fujirebio Holdings, Inc., President and CEO

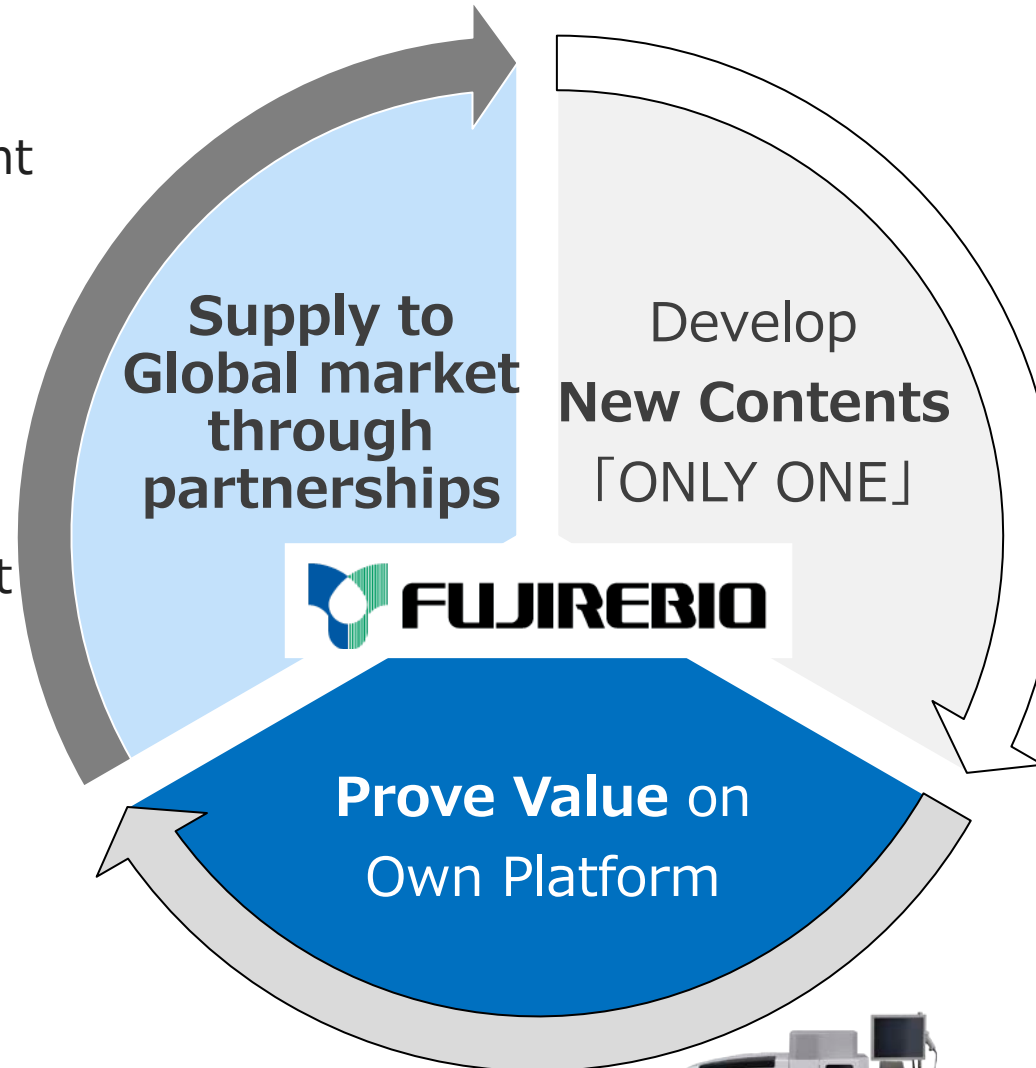
Goki Ishikawa

Progress of Strategy (Overview)

CDMO agreements

for contract development and manufacturing with IVD players having immunoassay analyzer installed base

- **7 Partners** for contract development and manufacturing
- Ab supply: Many



15% Base Revenue

spend on R&D activities

- Focus on Immunoassay

Global R&D Team,

300+ members in JPN/EU/US

- **20%+** of total employees

2 newly acquired companies

integrated fully into the group

- Part of our growth strategy



Develop and launch **quickly**

- RUO to IVD approach



ADx and Fluxus successfully integrated into the group



ADx creates tailor-made antibodies and assays in the Neuro field.



Fluxus develops Ultrasensitive Detection Technology based platform.

- No employees left the company because of acquisition.
- R&D teams across entities are collaborating day-to-day in our Global R&D team.
- CDMO discussions ongoing based on “FUJIREBIO strategy” incorporating both companies.

Pursue **Synergies** in FUJIREBIO strategy while keeping both companies' **Entrepreneurial Culture**

Our Approaches

Life Science / RUO market
Pharma and Research institutions etc.

LUMIPULSE



Speed-up the expansion of **Neuro markers** line-up.



Ultrasensitive Detection



Identify areas where Ultrasensitive Detection can add clinical values, and accelerate reagent development



In Vitro Diagnostics Market
Medical institutions etc.

Regulatory applications for selected markers (e.g. FDA)

- Subsidiaries experienced in regulatory affairs (Clinical trials, Regulatory registration)

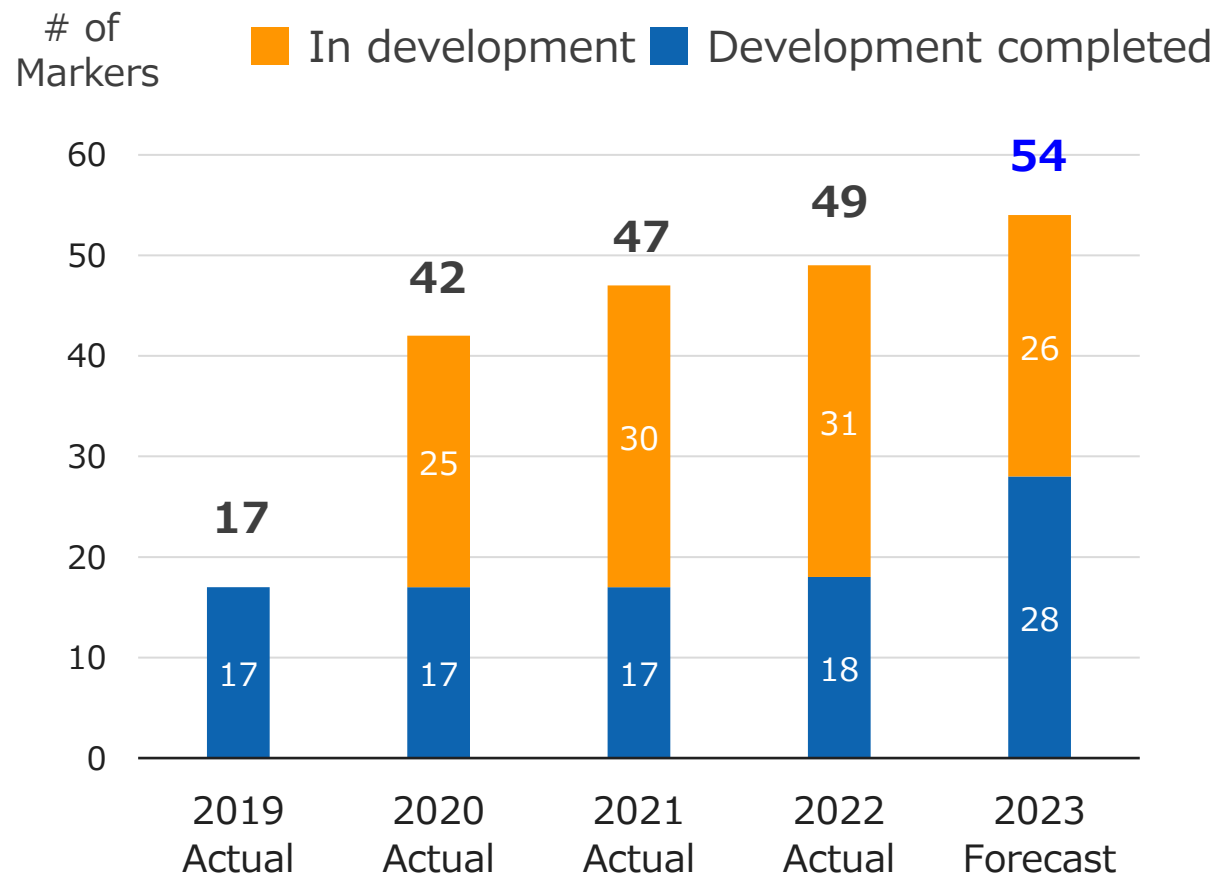
Regulatory applications for selected markers and the instrument (e.g. FDA)

- Advance the development of improved high-throughput versions

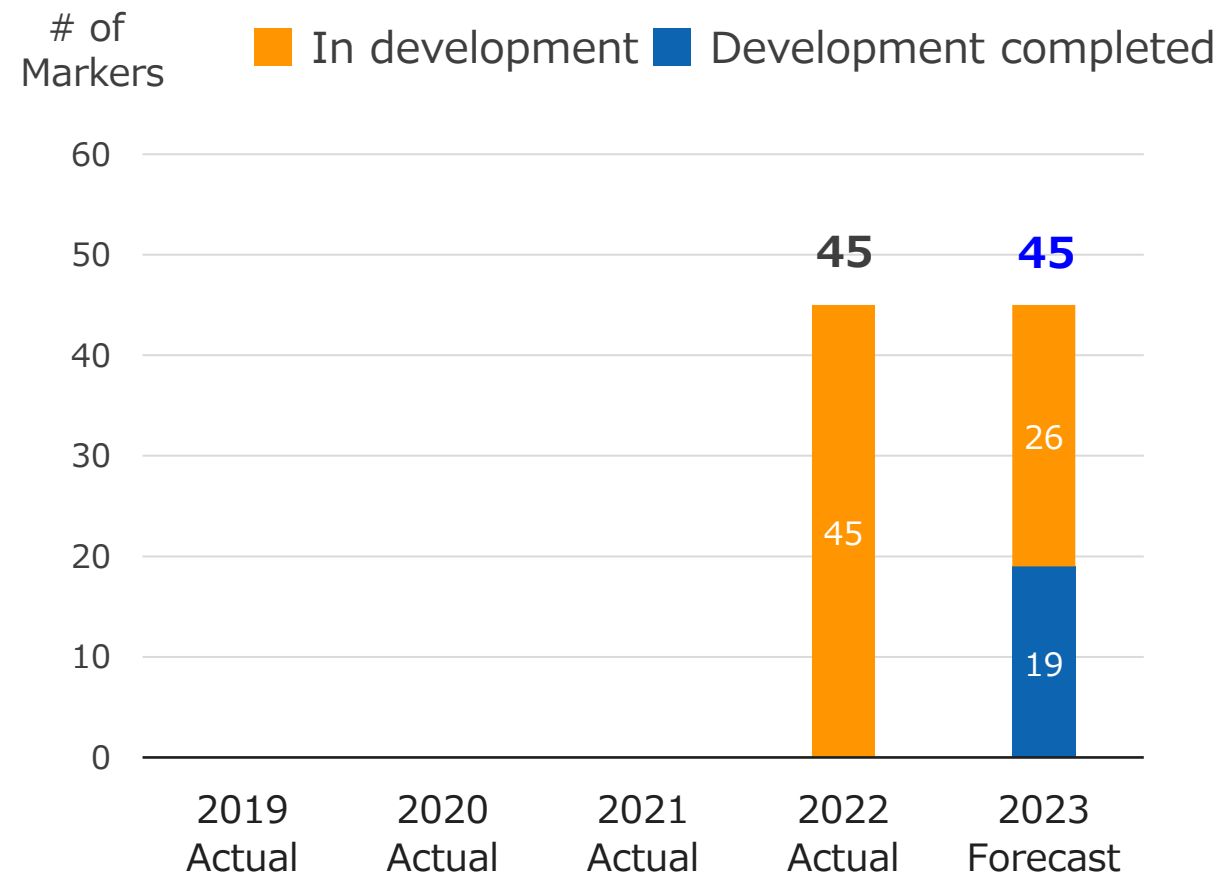
Aim to expand our business in two markets, "RUO" and "IVD", by leveraging CDMO business model

Progress of KPI : Accumulated # of Markers (Reagent)

Global Partners

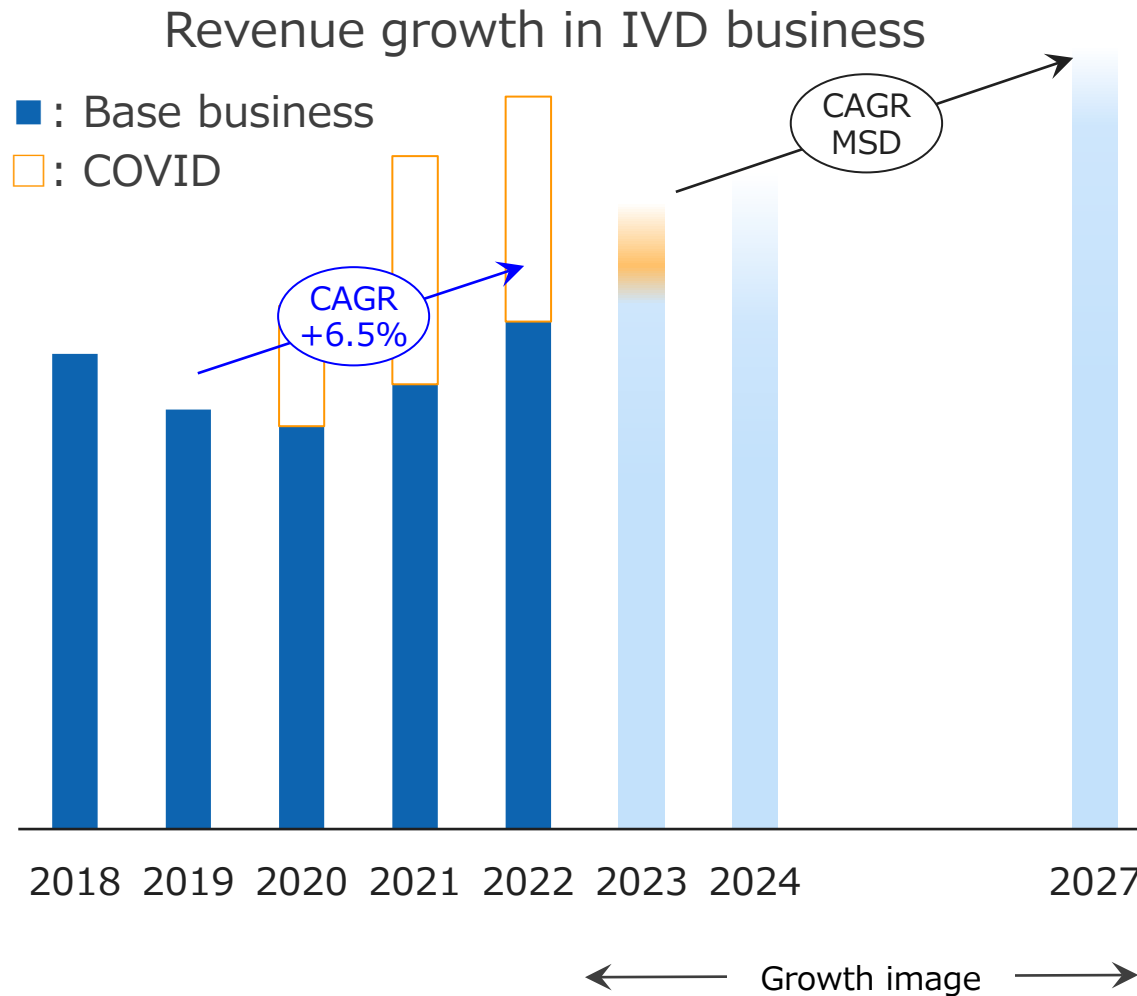


Regional Partners



A number of Neuro related markers are expected to be signed as new contract development projects in 2023

Growth scenario Post-COVID



“Base business” will continue to grow steadily

- “Base business” excluding COVID has grown by +6.5%/year since FY2019
- Aiming at continuous Mid-Single Digit growth

CDMO will lead our growth in mid and long term based on our strategic and multitiered initiatives

1. Steady growth in Reagent manufacturing and Raw material supply in “Oncology field”
2. Start of Reagent manufacturing of new development projects gained since 2020
3. New CDMO deals in **Neuro field** from 2023 (expected to complete development in 2025)
4. New CDMO deals for **Ultrasensitive Detection**

Focus on Neuro field and Ultrasensitive Detection where our CDMO business is expected to grow

R&D Activities and CDMO Business in Neuro/Alzheimer field

Fujirebio Holdings, Inc., Board Member (Neuro Business)
Fujirebio Europe NV, CEO
Christiaan De Wilde

ADx NeuroSciences, CEO
Koen Dewaele



Board Member, Fujirebio Holdings Inc.
Fujirebio Europe NV, CEO
Christiaan De Wilde

- 15+yrs, J&J/Janssen Pharmaceuticals
 - CFO, Janssen-Cilag Belux
- CEO, Innogenetics/Fujirebio Europe (2007~)

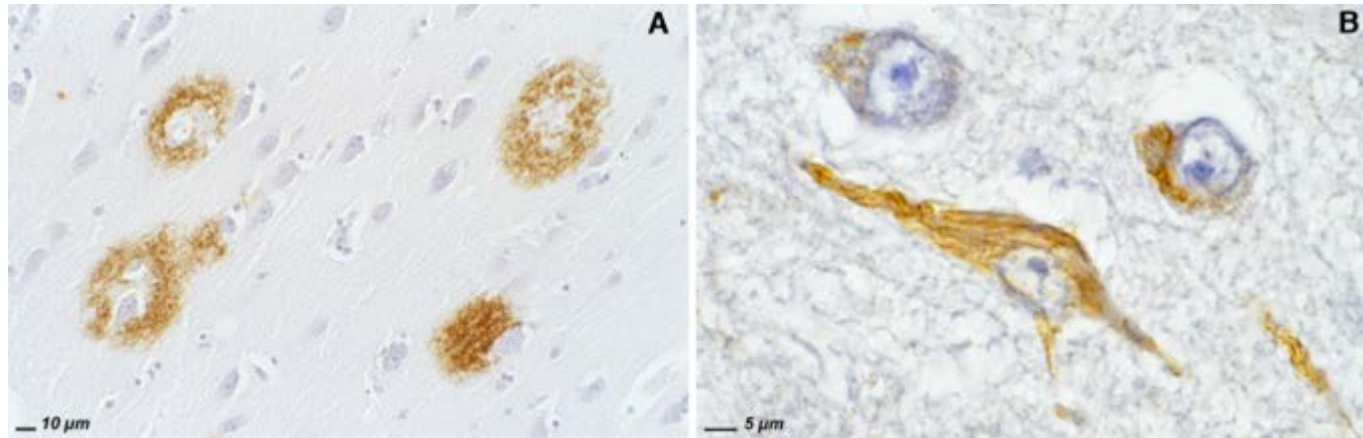


ADx NeuroSciences, CEO
Koen Dewaele

- 35+yrs, in In Vitro Diagnostic business
- 10+yrs, Innogenetics
 - Various positions (Marketing etc.)
- Founder & CEO, ADx NeuroSciences (2011~)

Alzheimer's Disease Pathology

Micro

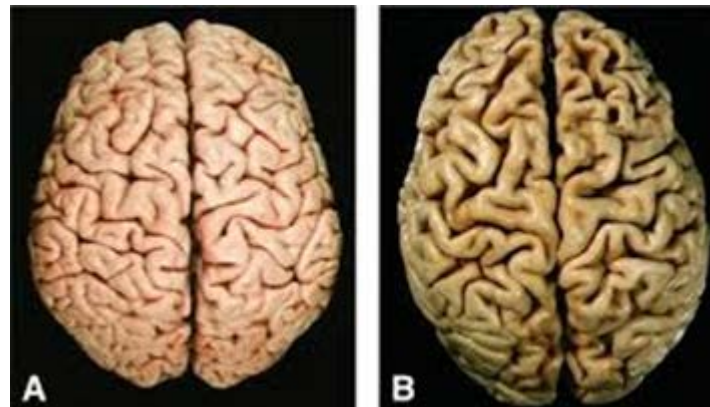


Source:
Le Bastard et al., 2009
CML-Neurology

A. Amyloid plaques identified in the hippocampus with 4G8 immunohistochemistry (40x)

B. Neurofibrillary tangles identified in the hippocampus with NFT200 immunohistochemistry (100x)

Macro

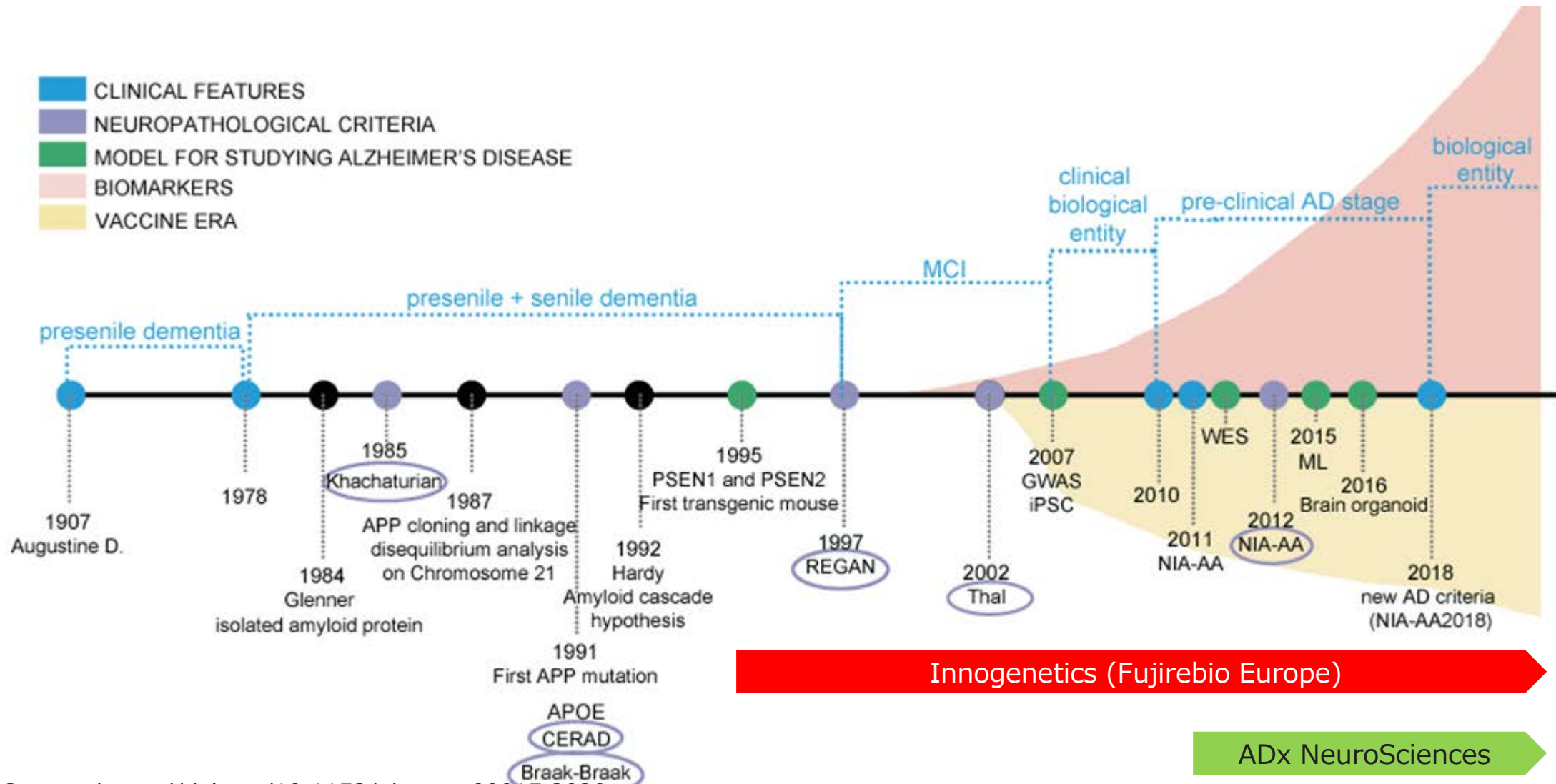


A. Normal brain

B. Atrophic brain

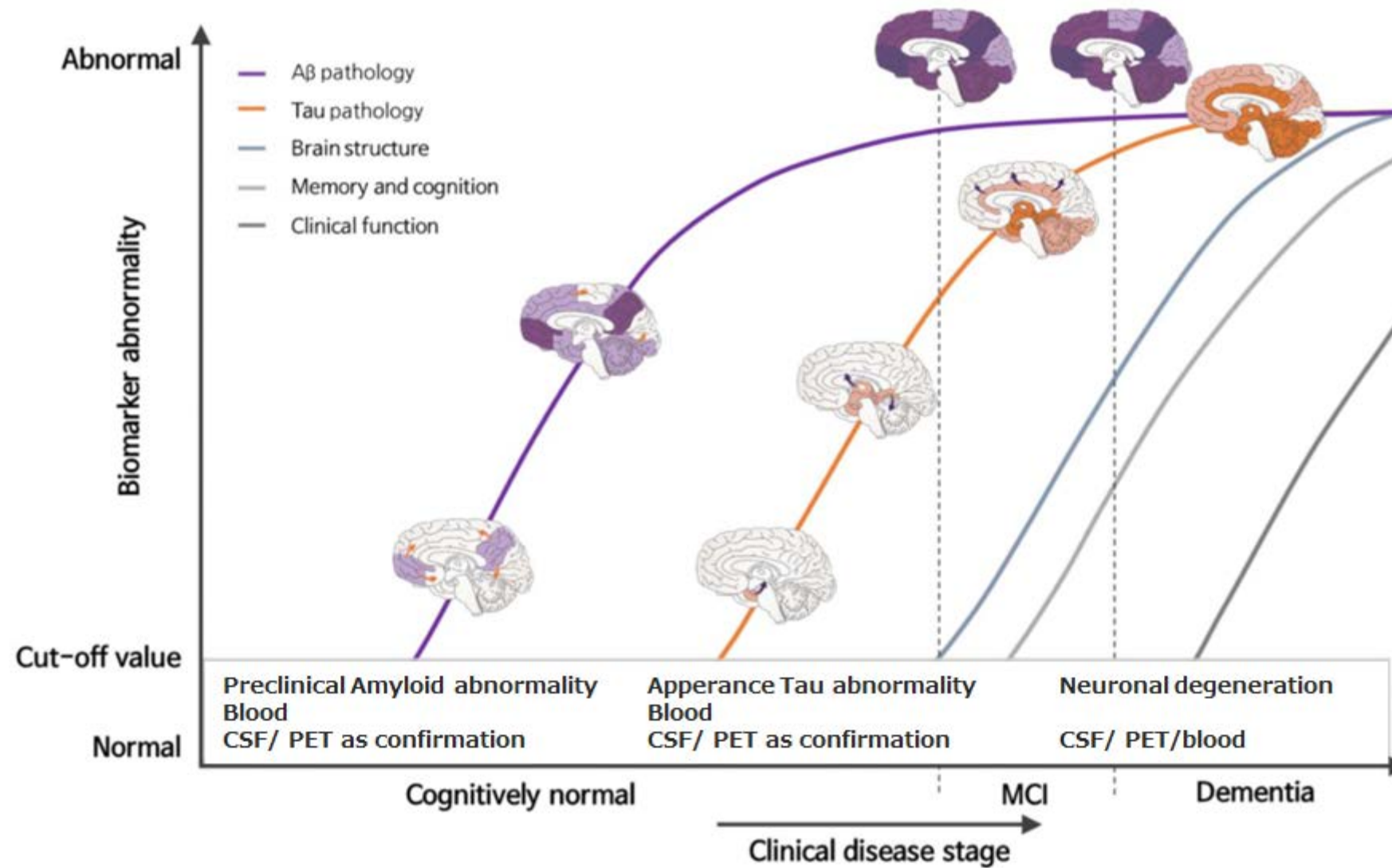
Source: <http://journals.lww.com/neurotodayonline/blog/breakingnews/pages/post.aspx?PostID=363>

History of Alzheimer's Diagnosis



Source: <https://doi.org/10.1152/physrev.00015.2020>

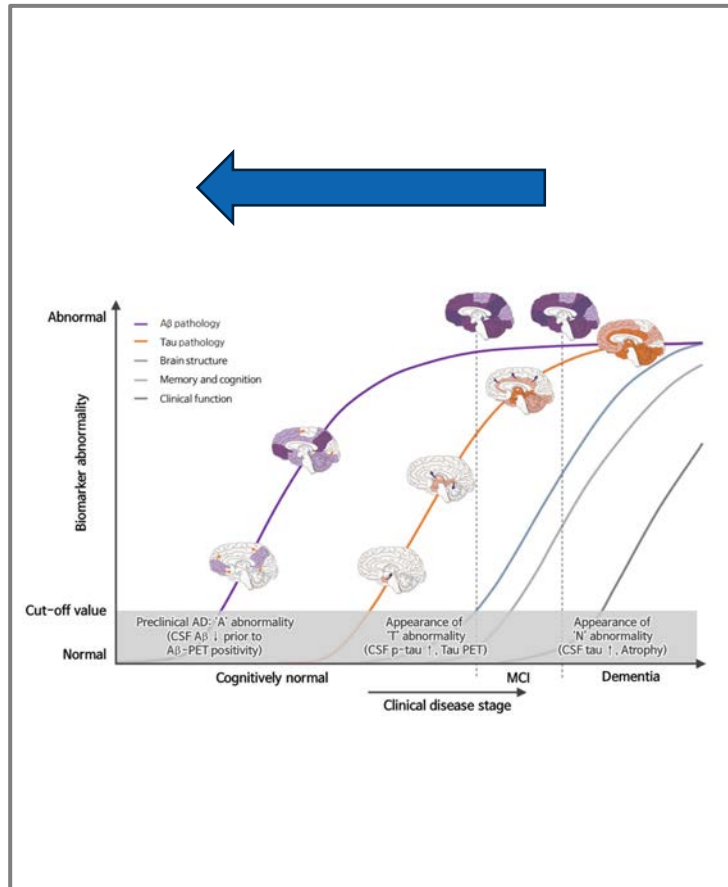
Biomarker changes during the disease process



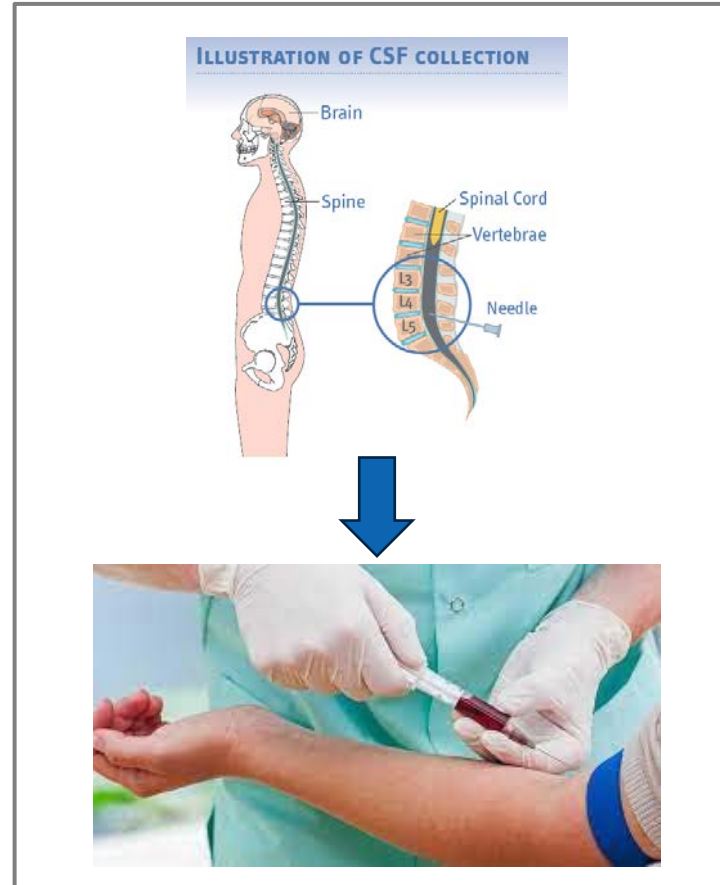
Source: <https://doi.org/10.3390/biomedicines10040850>

Trends in Neurobiomarker Testing

Early Detection



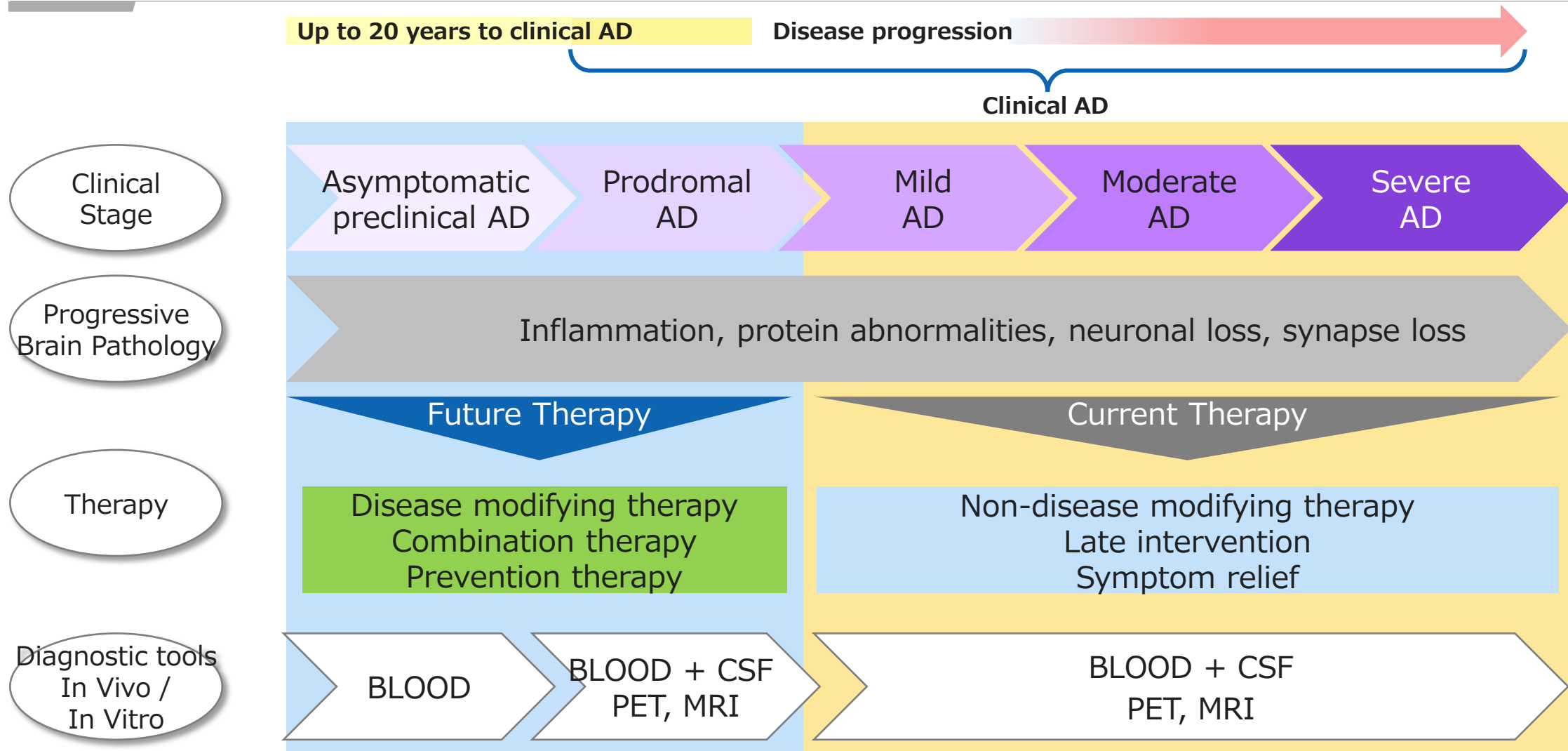
From CSF to Blood



Ultrasensitive

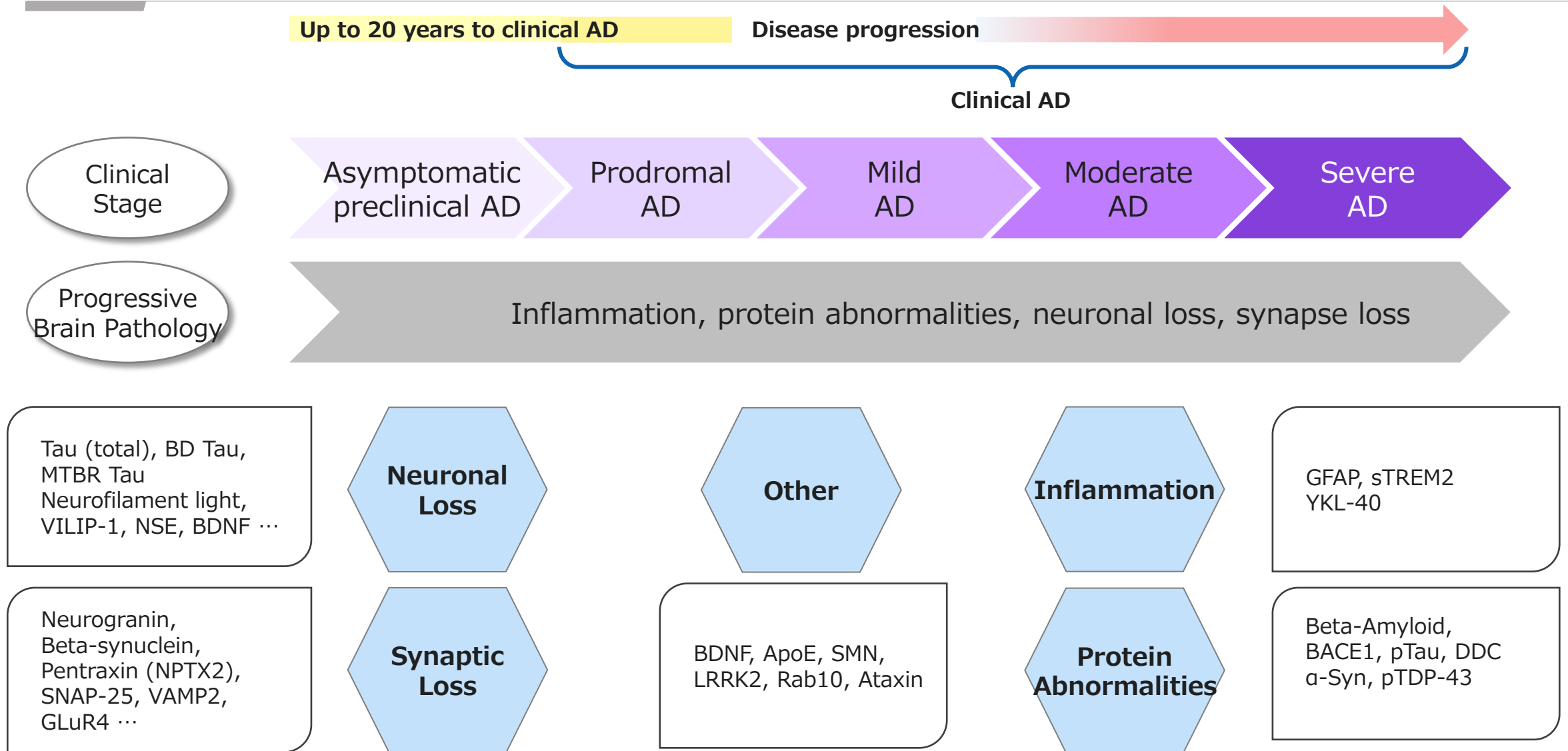
Submultiples		
Value	SI symbol	Name
10^{-1} g	dg	decigram
10^{-2} g	cg	centigram
10^{-3} g	mg	milligram
10^{-6} g	μg	microgram
10^{-9} g	ng	nanogram
10^{-12} g	pg	picogram
10^{-15} g	fg	femtogram
10^{-18} g	ag	attogram
10^{-21} g	zg	zeptogram
10^{-24} g	yg	yoctogram

Effective therapies will need specific biomarkers

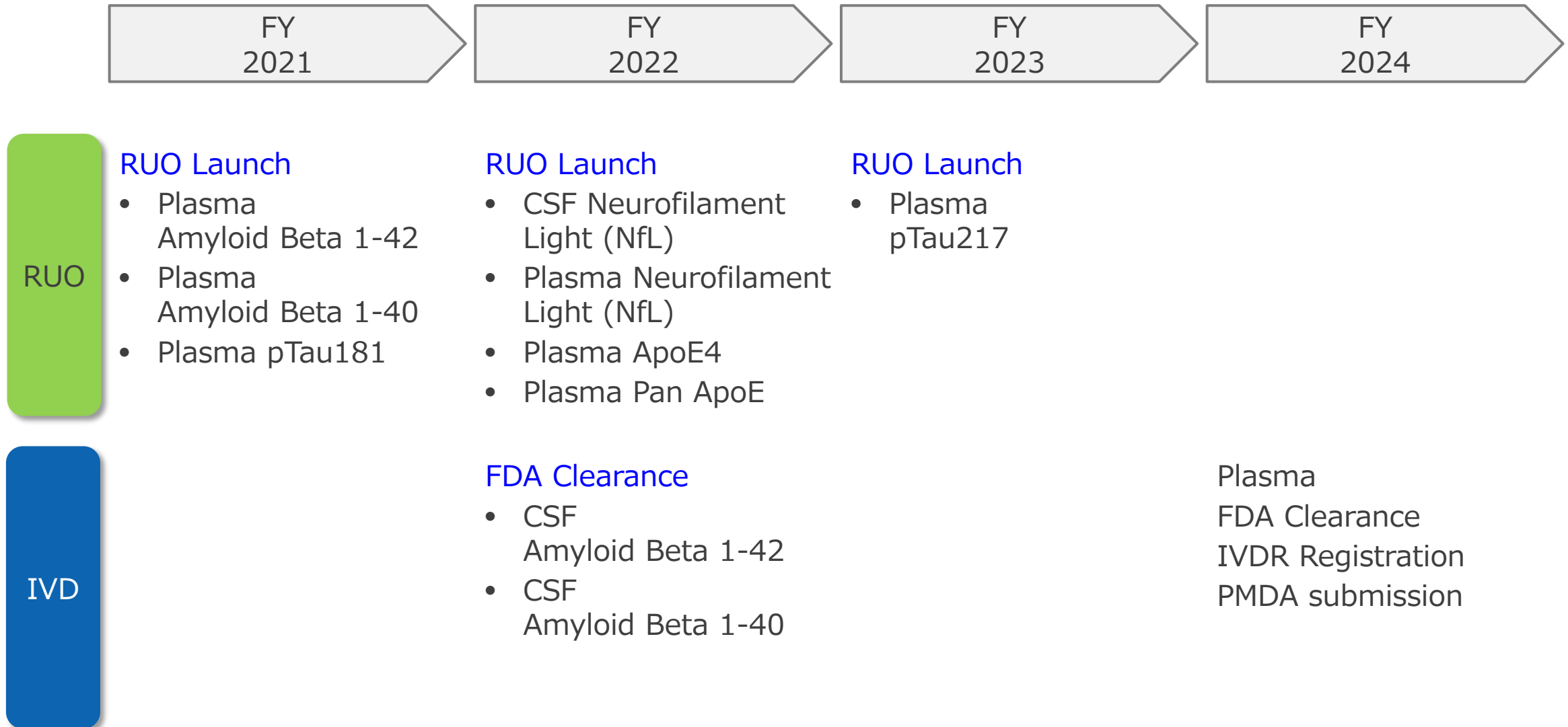


Biomarkers are needed for pharma to select the right patients and the most effective therapy

Specific biomarkers for neurodegeneration

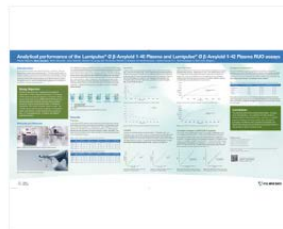


Neuro – Fujirebio Assay Development Road Map



Publications - Broad International Scientific Coverage

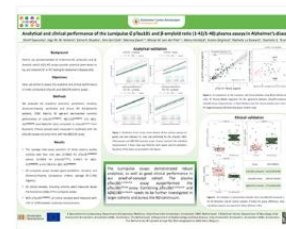
> 25
Posters on
international
conferences



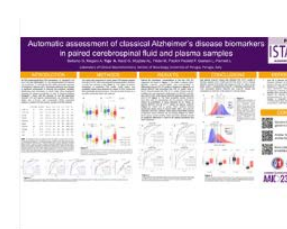
AAIC 22 Lumipulse
G-B-Amyloid...



AAIC 22 Lumipulse
G-pTau Plasma



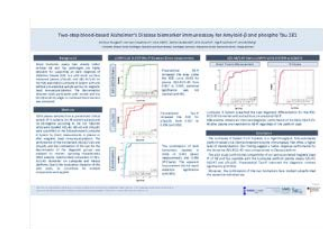
Bayoumy et al
Amsterdam UMC...



LPS plasma
pTau181 and AB...



LPS plasma
pTau217 poster...



Morgado et al
Göttingen...

> 15
Peer reviewed
scientific
articles



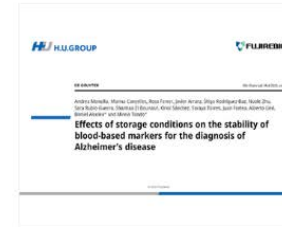
2022 Wilson et al -
Alzheimers Res...



2022 Wilson et al -
Alzheimers Res...



2023 Mansilla et al -
Clin Chem Lab M...



2023 Mansilla et al -
Clin Chem Lab M...



2023 Verde et al -
Neurol Sci...



2023 Verde et al -
Neurol Sci (ppt...

> 10
Oral presentations
on international
conferences



Study principle



Study coordinators

Dr. Alberto Lleo & Dr. Daniel Alcolea
Hospital Sant-Pau, Barcelona, Spain

Study set-up

- Plasma samples selection from the clinic
 - 20 A-T- cognitively healthy
 - 30 A+T+ prodromal AD
(Mild Cognitive Impairment)
 - 20 A-T- non-neurodegenerative MCI
(MCI not linked to AD or other degenerative diseases)
 - 31 A+T- symptomatic individuals
(heterogenous group of clinical diagnosis)
- Assays included
 - Lumipulse G pTau 217 Plasma
 - Lumipulse G pTau 181 Plasma
 - Lumipulse G Amyloid Beta 1-42 Plasma
 - Lumipulse G Amyloid Beta 1-40 Plasma

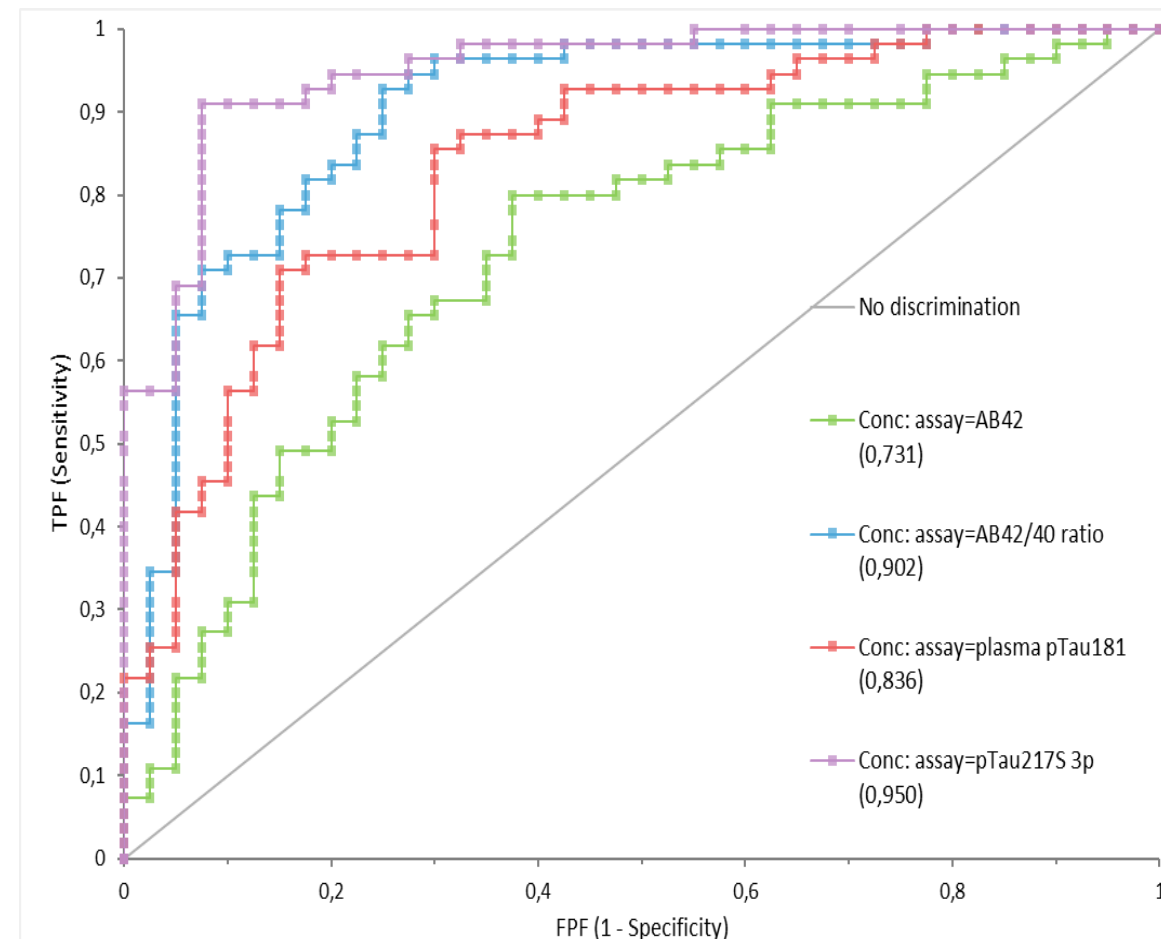
Ability LMP assays to categorize samples correctly by Area Under the Curve (AUC)

- Amyloid positive (**A+**) from Amyloid negative (**A-**)
- Amyloid positive/Tau positive (**A+T+**) from Amyloid negative/Tau negative (**A-T-**)

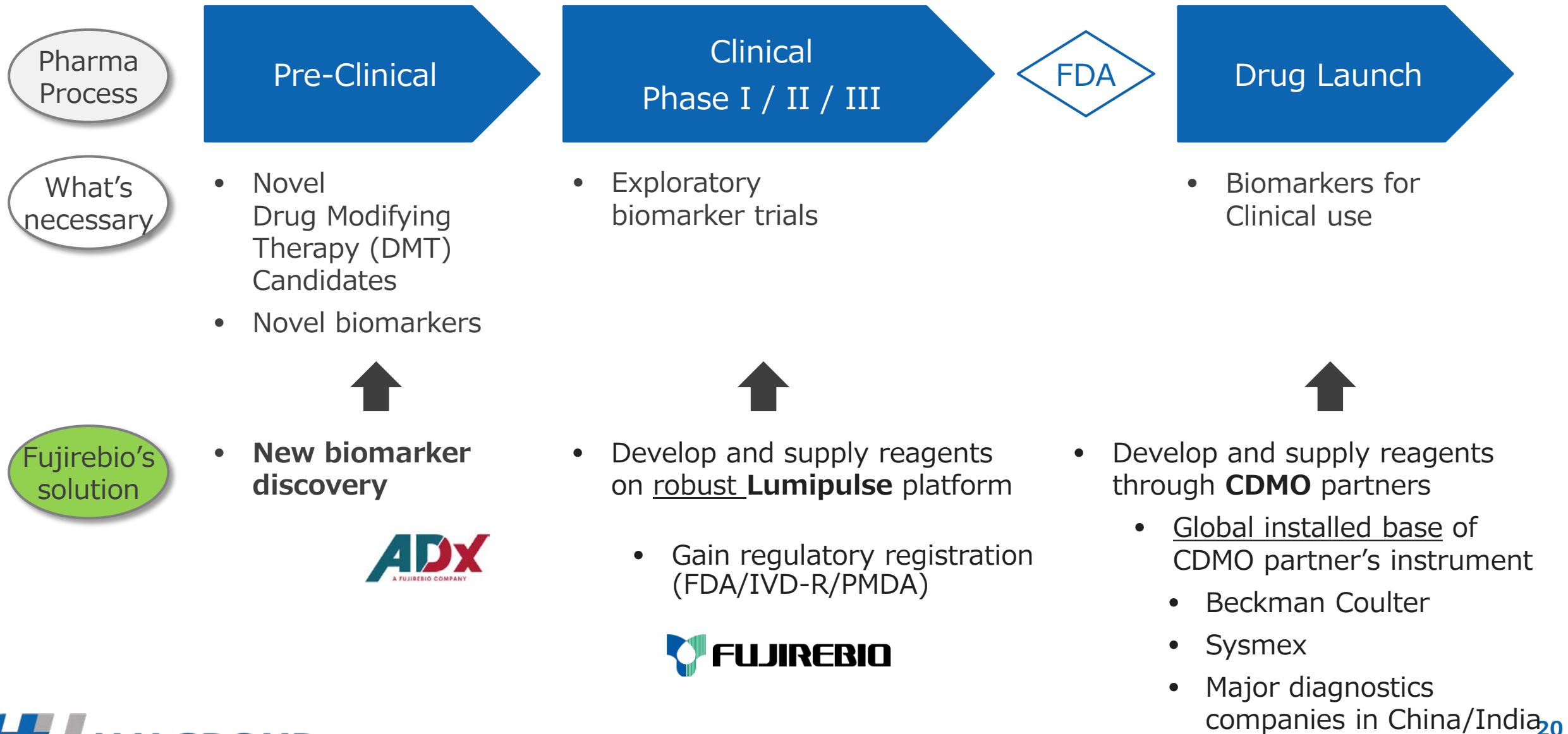
Assay	AUC (A+/A-)	AUC (A+T+/A-T-)
Lumipulse G pTau 217 Plasma	0,95	0,99
Lumipulse G pTau 181 Plasma	0,84	0,86
Lumipulse G AB42/40 Plasma	0,90	0,90

A+: n = 55 A+T+: n = 31
A-: n = 40 A-T-: n = 30

Clinical performance LMP assays by AUC (A+ vs A- samples)



Fujirebio's Value Story



SUMMARY

- There is huge portfolio of neurodegenerative disease biomarkers
 - We will expand our biomarker portfolio from Amyloid Beta, pTau, NfL etc.
- Fujirebio aims to develop novel biomarkers on a robust system, LUMIPULSE
Since 2021, we are successful in developing and registering new markers
- Fujirebio's reagents show highest level of performance compared to other players in market
- Fujirebio can support the community through broad range of solutions
 - With ADx NeuroSciences joining Fujirebio, we can provide comprehensive solutions to pharmaceutical companies who need biomarkers for their drug development
- LUMIPULSE & CDMO strategy can contribute to preparing necessary testing capacity globally
 - Our Neuro CDMO partners have strong footprint on a global scale; Beckman Coulter, Sysmex and major diagnostics companies in China and India
- Our global team is committed to grow the diagnostic market for neurodegenerative disease

Ultrasensitive Detection Technology and CDMO Business

Fujirebio Holdings, Inc., Board Member (R&D)
Katsumi Aoyagi Ph.D.

Fluxus Inc., CEO
Peter Wagner Ph.D.



Board Member, Fujirebio Holdings Inc.
Managing Director, Fujirebio, Inc.
Katsumi Aoyagi Ph.D.

- Ph.D. (Tohoku University)
- CEO, Advanced Life Science Institute, Inc. (2017~)
- Board member (R&D), Fujirebio, Inc.(2016~)

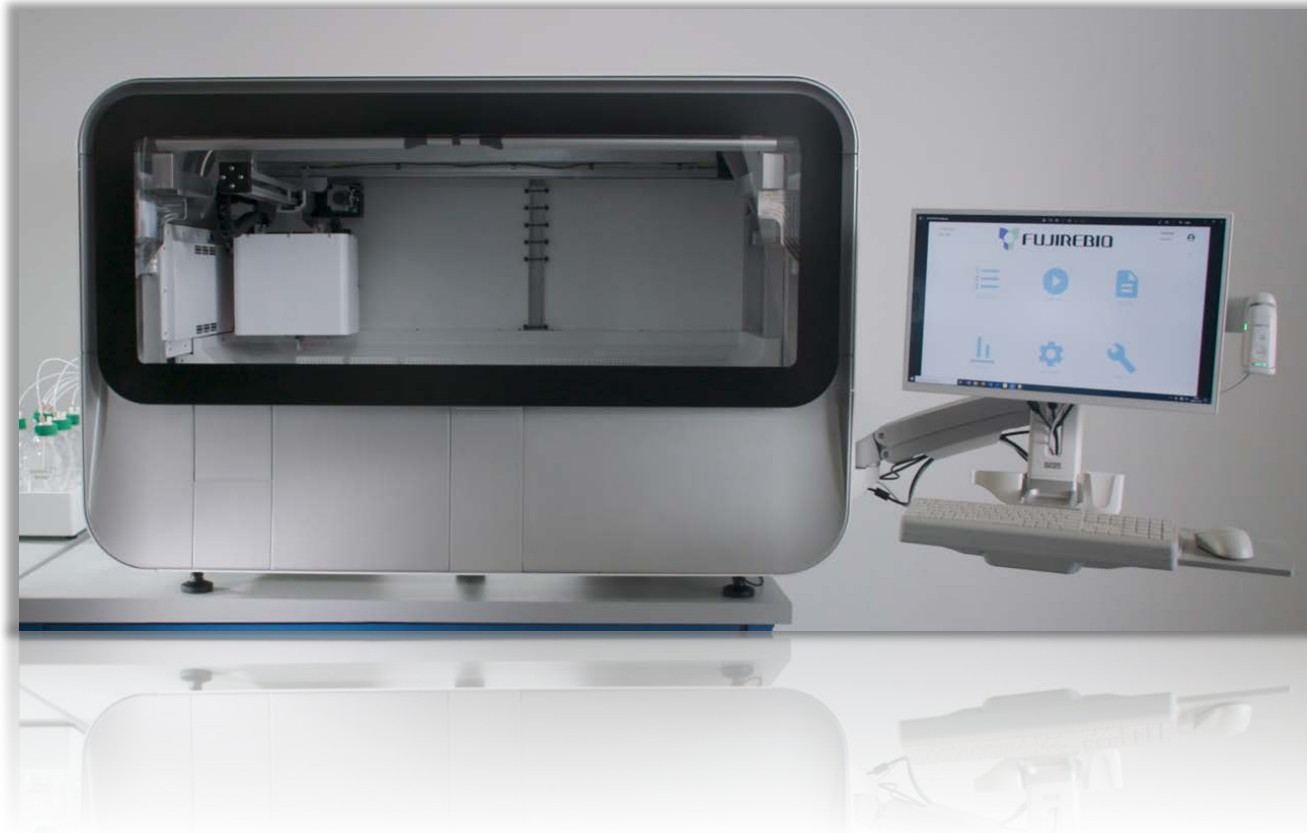


Fluxus Inc., CEO
Peter Wagner Ph.D.

- 26+yrs experience in Life Science tools and IVD
- Founder and CEO, Zyomyx Inc. (15+yrs)
- Founder and CEO, Fluxus Inc. (2016~)



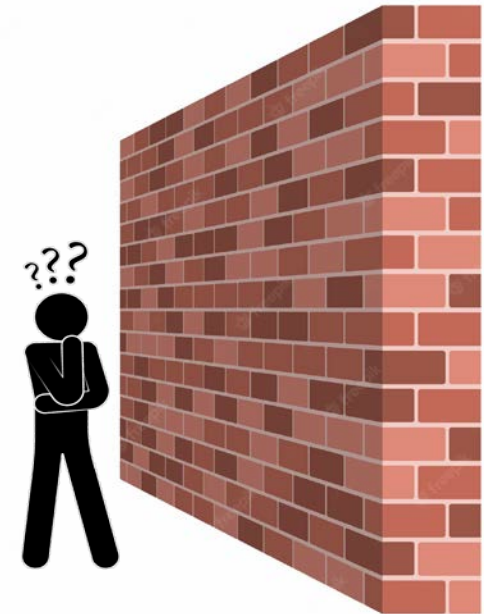
- Fluxus, located in Silicon Valley, California, co-developed Ultrasensitive Detection technologies with Fujirebio for the past 6 years.
- Fluxus was acquired by Fujirebio HD in July 2022.
- At IR Day 2022, Fluxus was announced with the promise of launching an ultrasensitive analyzer in early 2024.
- As promised, I would like to introduce to you the new Fujirebio ultrasensitive analyzer system which will be launched in early 2024.



- **Fully Automated:**
Walk-away sample-to-answer processing
- **Ultrasensitive:**
Integrated UDM detection system for single-molecule counting
- **Efficient:**
Up to 48 assays per batch run, multiple formats in parallel
- **Flexible:**
Accommodates a wide variety of assay conditions and analytes

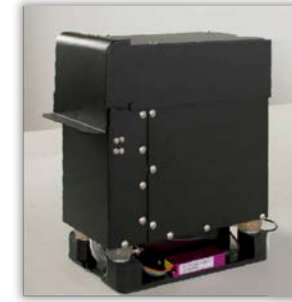
Why Ultrasensitivity?

- Conventional immunoassay methods have reached their limits of sensitivity and dynamic range.
- Market demand for ultrasensitive technologies is increasing - particularly in neurology infectious disease, and oncology testing.
- Higher sensitivity enables:
 - New clinical utility
 - Discovery of new markers at lower levels in all fields
 - Earlier detection and diagnosis
 - Infectious disease, oncology
 - Use of less invasive sample types
 - Infectious disease marker in urine, saliva, etc.
 - Lower volume consumption = more tests per sample



Fluxus Technology – Key Components

- Universal Detection Module (UDM)



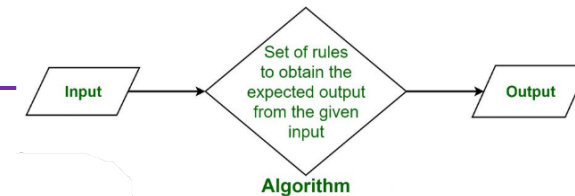
- Optofluidic Cartridges



- High Performance Reagents & Assays



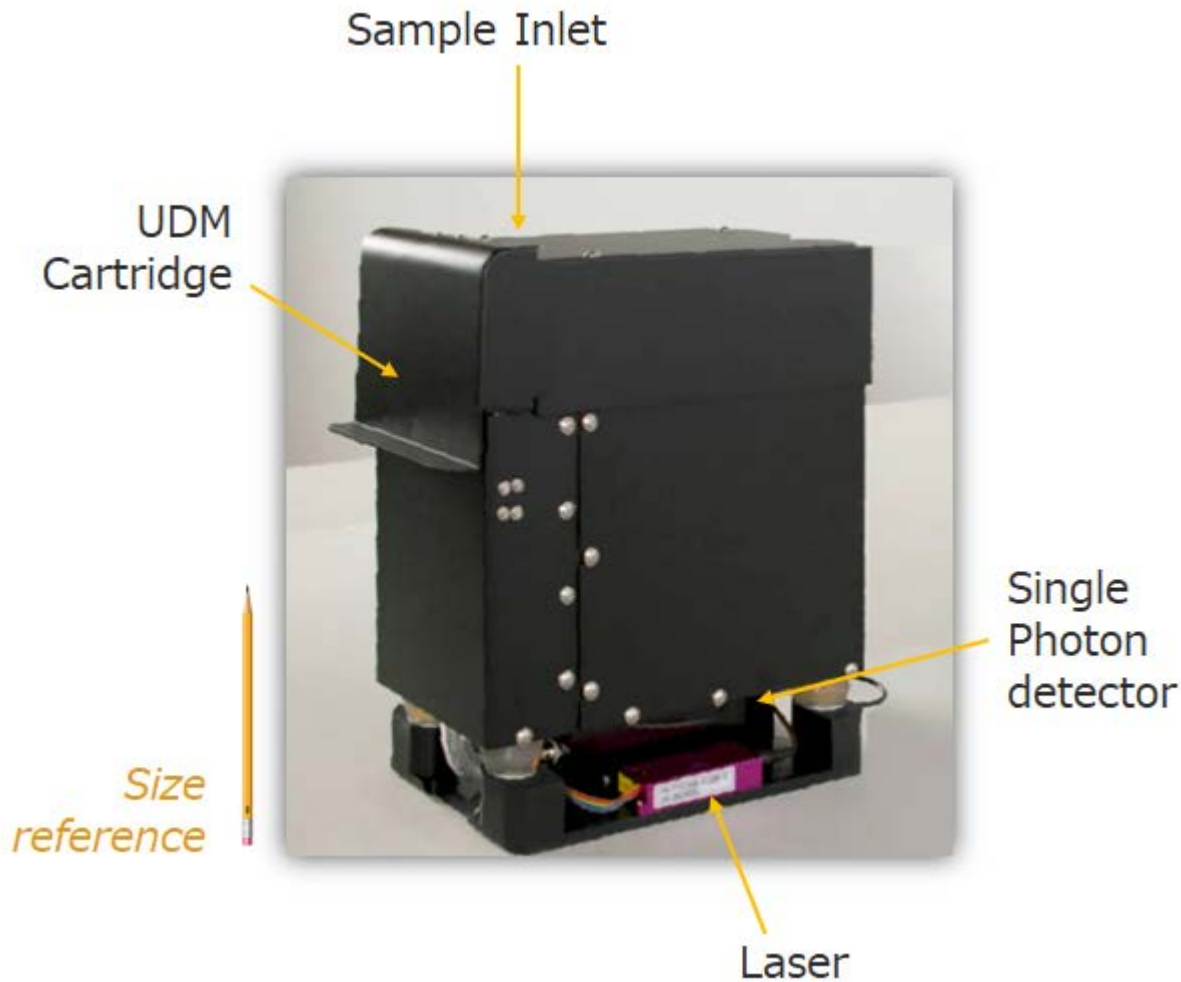
- Data Analysis Algorithms



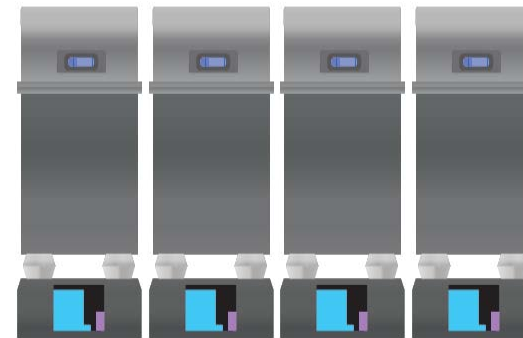
- Ultrasensitive Analyzer (RUO)



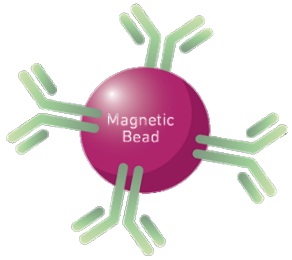
Universal Detection Module (UDM)



- Single molecule detection
- Incorporates replaceable optofluidic UDM Cartridge
- Sample injection with automated pipettor
- Small footprint for integration into any system
- Stackable to accommodate any throughput:



1x ~ 60 tests/hour
 2x ~ 120 tests/hour
 3x ~ 180 tests/hour
 4x ~ 240 tests/hour



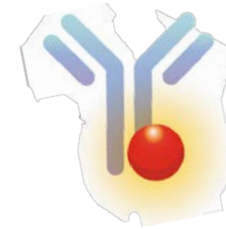
Fujirebio Reagents

- Industry leader in the identification and supply of novel antibodies



Single Test Cartridges

- Same concept as LUMIPULSE G1200
- High precision, reproducibility
- Fujirebio manufacturing expertise



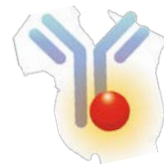
Fluxus Reporter

- Proprietary fluorescent dye-carrier construct
- Conjugated to detection antibody

Easy Adaptation of Pre-Existing Assays

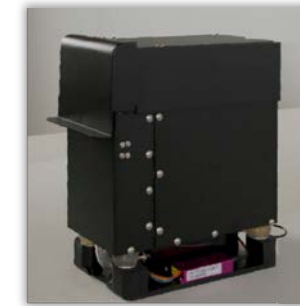
Existing
Immunoassay

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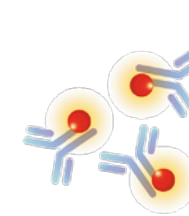
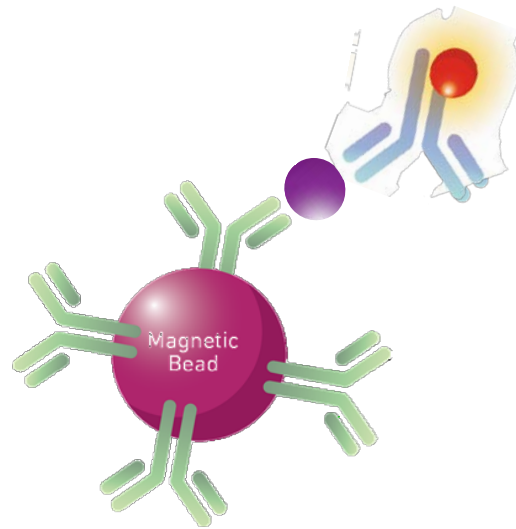


Fluxus Reporter

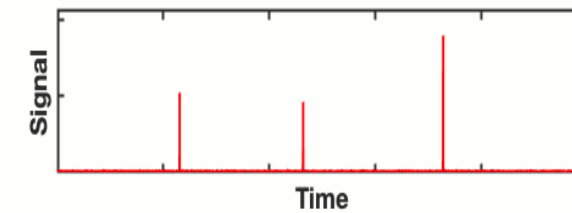
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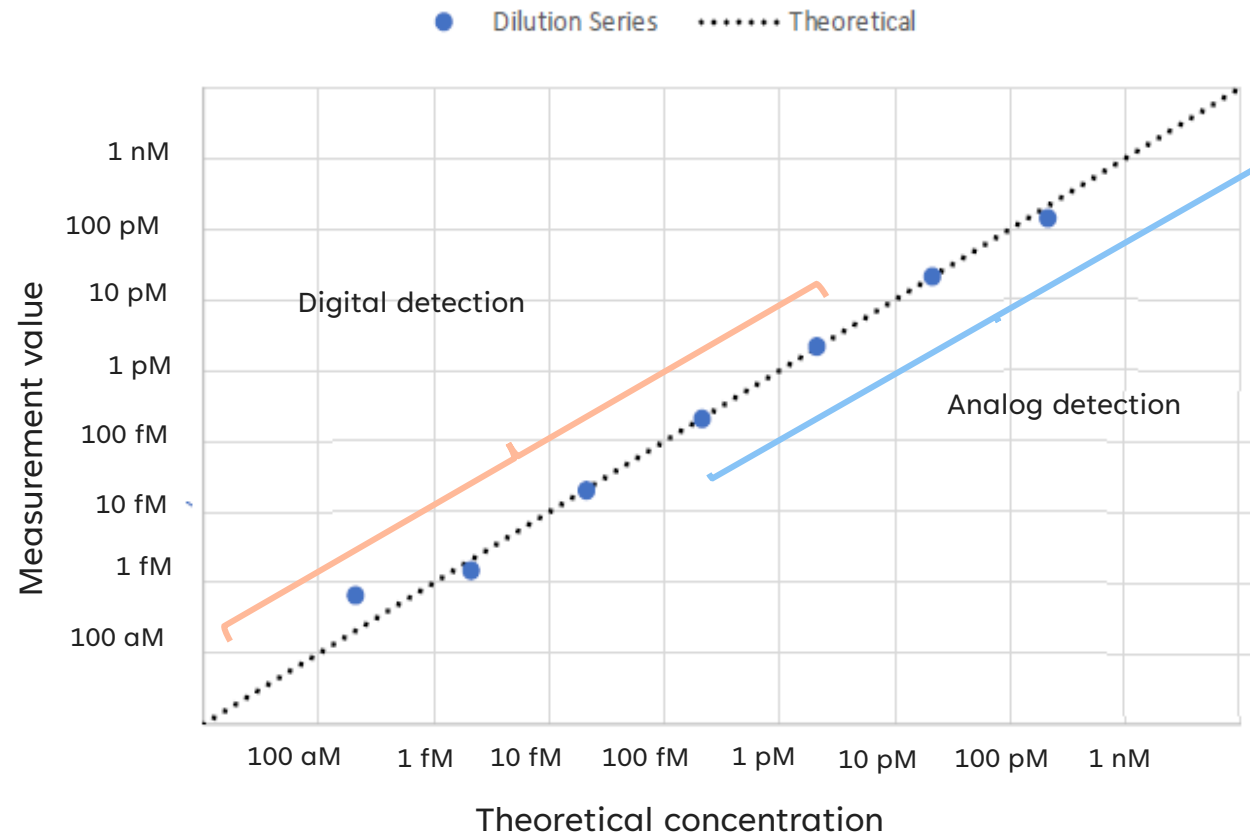
UDM



Single Molecule
Detection

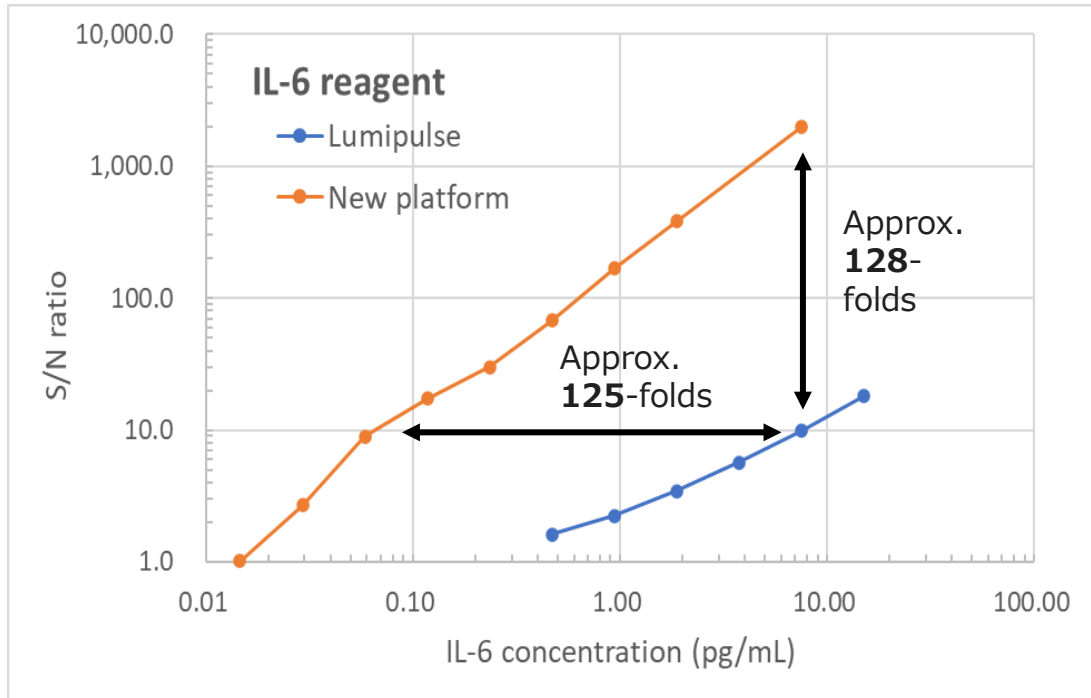


Detection Sensitivity and Dynamic Range

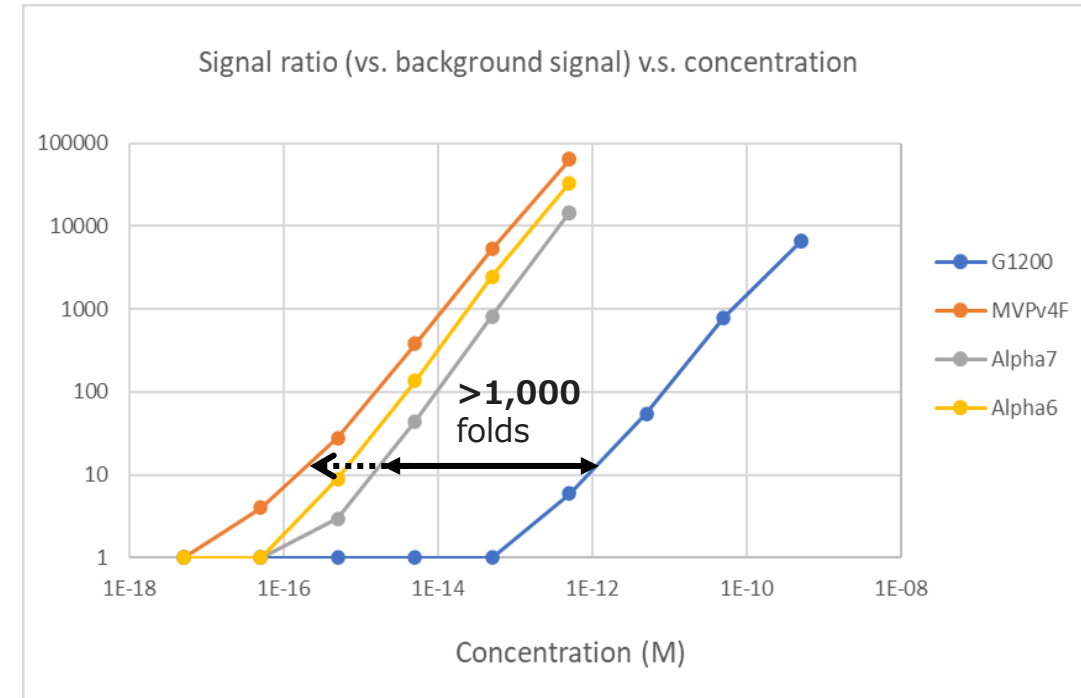


- Linearity: 100 aM ~ 1 nM
- Sensitivity: < 100 aM
- Dynamic range : > 7 Logs
Potentially > 9 Logs
< 100 aM - 100 nM

Typical example: IL-6 Assay



Detector performance using only measurement of diluted reporter conjugate (no immunoassay)



The new platform detector demonstrated the potential for **more than 1,000 times more sensitivity** than the LUMIPULSE G1200.

Future Roadmap

Launch RUO Analyzer and expand menu line-up (Neuro, Infectious diseases, Oncology etc.)



Bring to IVD (Analyzer and selected markers)

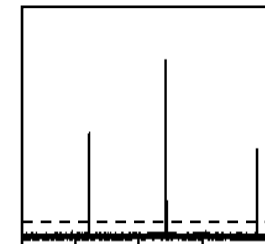
Licensing-out technology to be used for CDMO partner's next-generation immunoassay platform



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SUMMARY

- Fujirebio believes Ultrasensitive Detection will add huge clinical benefit for selected markers in immunoassay field.
- Fluxus has been developing the Ultrasensitive Detection system since 2017, through partnership with Fujirebio, with the intent to include in Fujirebio's future immunoassay platform.
- With the acquisition of Fluxus by Fujirebio HD in 2022, development of benchtop RUO analyzer and reagents has been accelerated, currently scheduled for launch in early 2024.
- Initial data shows high performance as expected. For selected markers, Fluxus RUO analyzer shows over 100 times higher sensitivity compared to LUMIPULSE.
- First wave of assays to be launched on RUO analyzer will be neuro biomarkers. Fujirebio will work on menu expansion beyond neuro into infectious disease and oncology, and also bring to IVD.
- This Ultrasensitive Detection technology will also be offered to our CDMO partners. Fujirebio is in discussion with multiple companies on licensing-out this technology and components.

QUESTIONS?