UCB Current and Future Leadership Perspectives in Epilepsy Treatment and Care

9th January 2023

Inspired by **patients.**
Driven by **science.**

Disclaimer and Safe Harbor

This presentation contains forward-looking statements, including, without limitation, statements containing the words "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guaranteeing future performance and are subject to known and unknown risks, uncertainties, and assumptions which might cause the actual results, financial condition, performance or achievements of UCB, or industry results, to be materially different from any future results, performance, or achievements expressed or implied by such forward-looking statements contained in this presentation.

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Our Global Epilepsy Leadership

Charl van Zyl
Executive Vice President, Neurology Solutions &
International Markets/Europe, UCB

Agenda

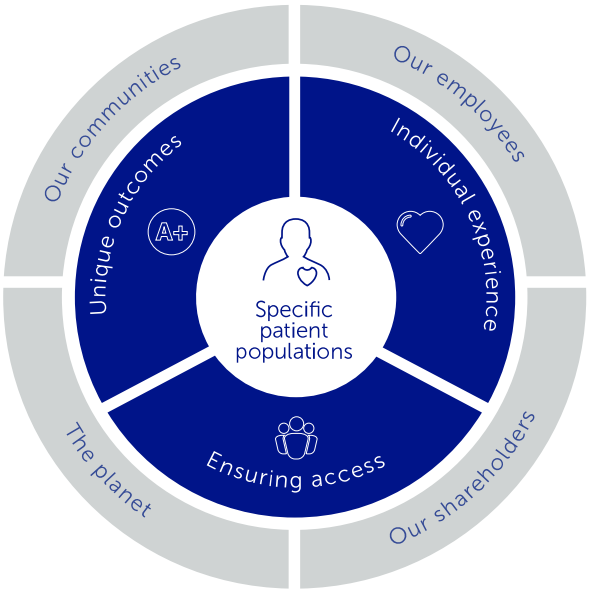
Antje Witte Head of Investor Relations, UCB	**Welcome**
Charl van Zyl Executive Vice President, UCB Neurology Solutions & Head of EU and International Markets	**Our Epilepsy Leadership**
Mike Davis Head of Global Epilepsy, UCB	**Our Unified Epilepsy Strategy**
Konrad Werhahn, MD PhD Head of Medical Affairs, Epileptologist, UCB	**Fintepla®▼ (fenfluramine oral solution) Provides a New Set of Answers in Dravet & Lennox Gastaut Syndrome**
Stefanie Dedeurwaerdere, PhD Head of Epilepsy Discovery, UCB	**Early Solutions: Leveraging Novel Science and Human Pathobiology for Improved Drug Targeting in Epilepsy**
Charl van Zyl Executive Vice President, UCB Neurology Solutions & Head of EU and International Markets	**Summary: Evolution of UCB's Epilepsy Pipeline into Precision Medicine with the Continued Ambition for Curative Therapy**
All Speakers	**Q&A Session**

Disclaimer: FINTEPLA is not approved in all geographies where we operate

Across UCB we are defined by our purpose:

Creating value for patients now and into the future

and sustainability is our business approach.



We believe that **everyone deserves to live the best life that they can** - as free as possible from the challenges and uncertainty of disease

UCB Epilepsy Leadership Across the Globe

~3.0M+
Epilepsy Patients under care worldwide

1 million
compounds per drug screening

>500+
protein targets reviewed AI/digital pathobiology framework

Worldwide epilepsy net sales
>€3.0B[1]

>250
interventional studies

>25,000
patients enrolled

UCB's Portfolio of Epilepsy Solutions

Keppra (levetiracetam) · VIMPAT (lacosamide) · BRIVIACT (brivaracetam) · Nayzilam (midazolam) nasal spray · Fintepla (fenfluramine)

Strategic Epilepsy Investments and Partnerships

Patient Solution Acquisitions
ZOGENIX · ENGAGE THERAPEUTICS

Drug Discovery Research
Transcriptomic Big Data Library in Epilepsy · GliaPharm · PRAXIS · Handl Therapeutics · Element Genomics · 5+

Digital Health
EYSZ · NextSense.io · nile · NEURAVA

[1]Full Year 2021: €3.238mn actual net sales as reported

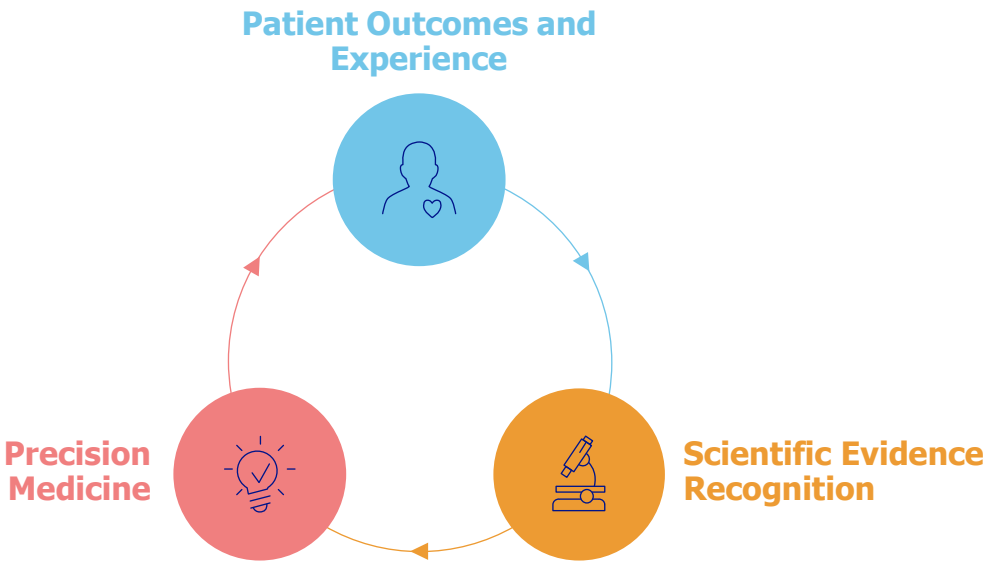
Our Unified Epilepsy Strategy

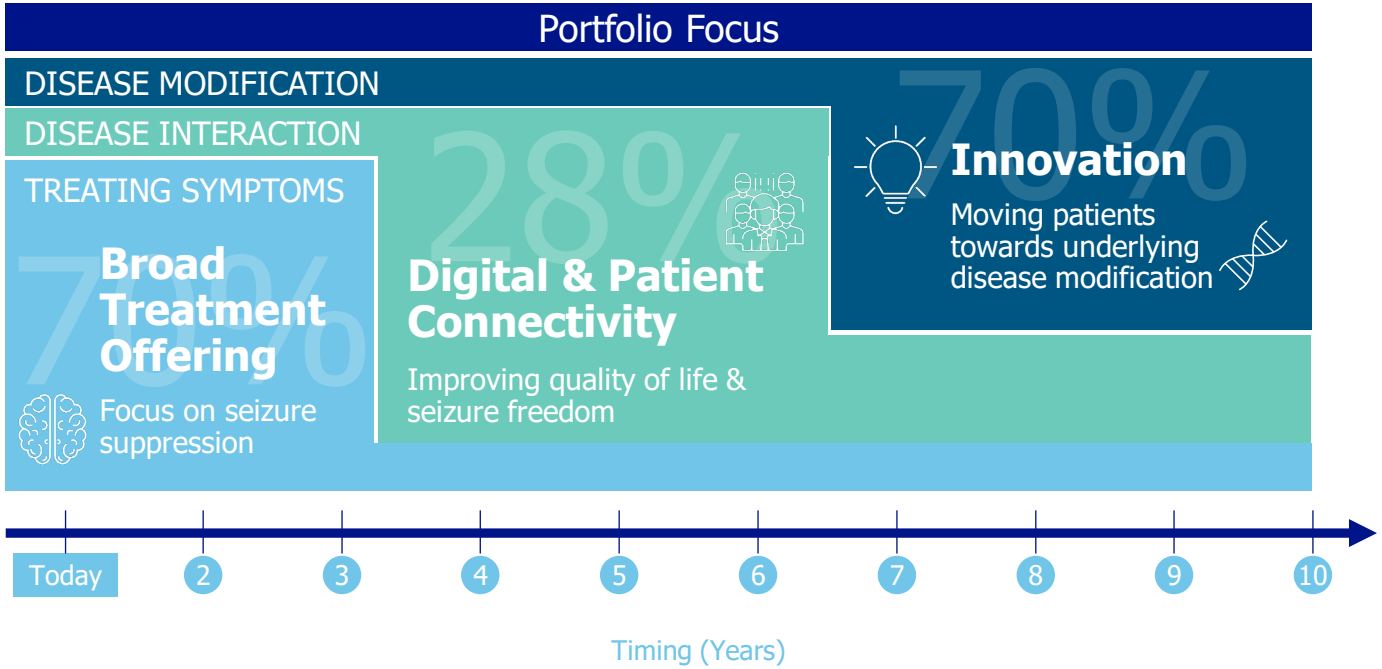
Mike Davis
Head of Global Epilepsy, UCB

Inspired by patients.
Driven by science.

Evolved UCB's Organization

To Better Care for People Living with Epilepsy and Rare Syndromes



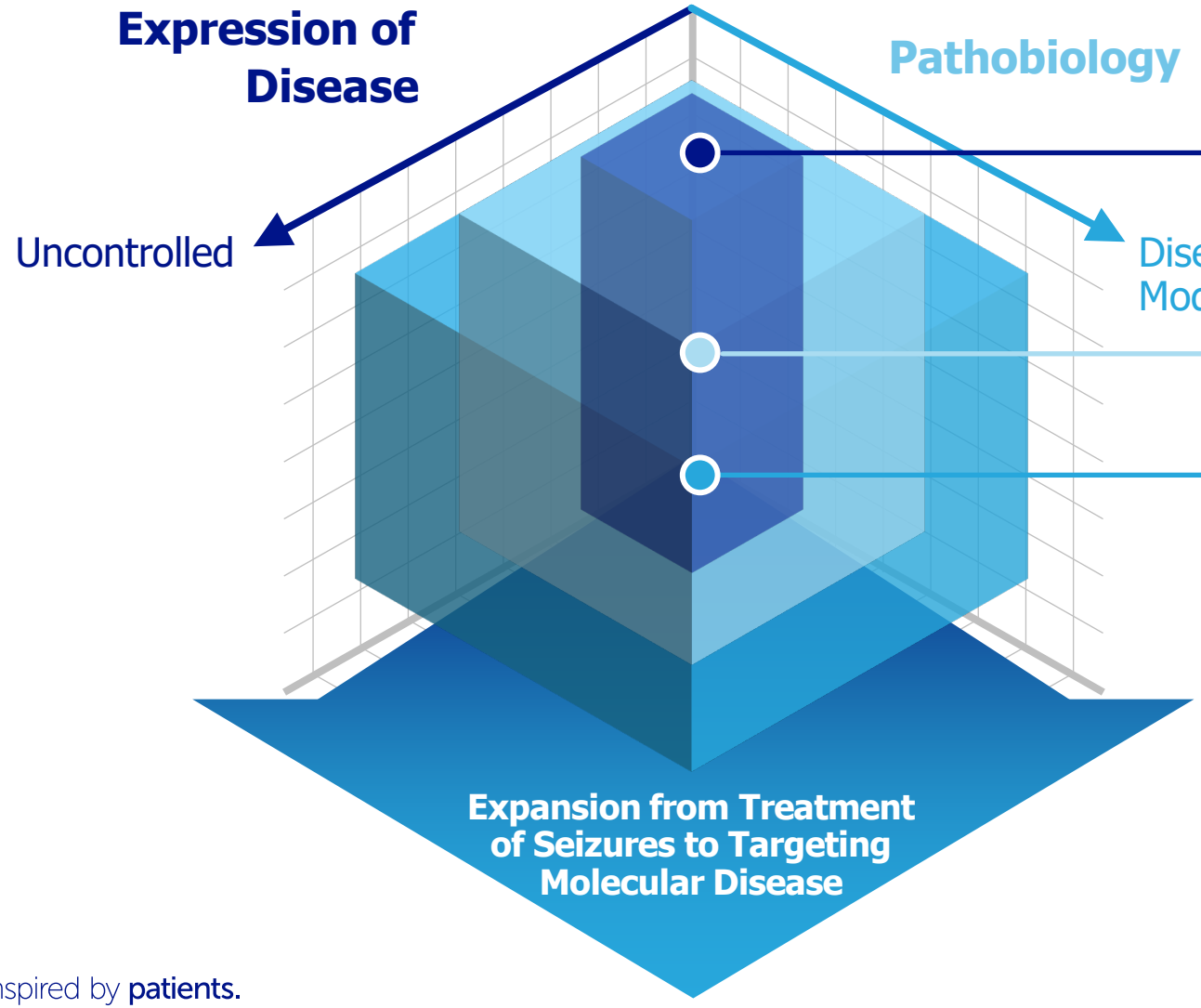


4 Key Drivers of Our Unified Epilepsy Strategy:

1. **Maximizing** – existing and future treatments
2. **Innovative Science** – new areas of science with a focus on specific unmet needs
3. **Digital Health** – investments to provide a more holistic level of treatment
4. **Sustainable Value** – driving access in a sustainable way; improving outcomes

Paradigm Shift from Seizure Suppression to Disease Modification

From Broad Populations to Expansion into Specific Populations with High Unmet Patient Needs



1 **TODAY**
Novel SV2A and Na+ Channel Agents
UCB Leading Role

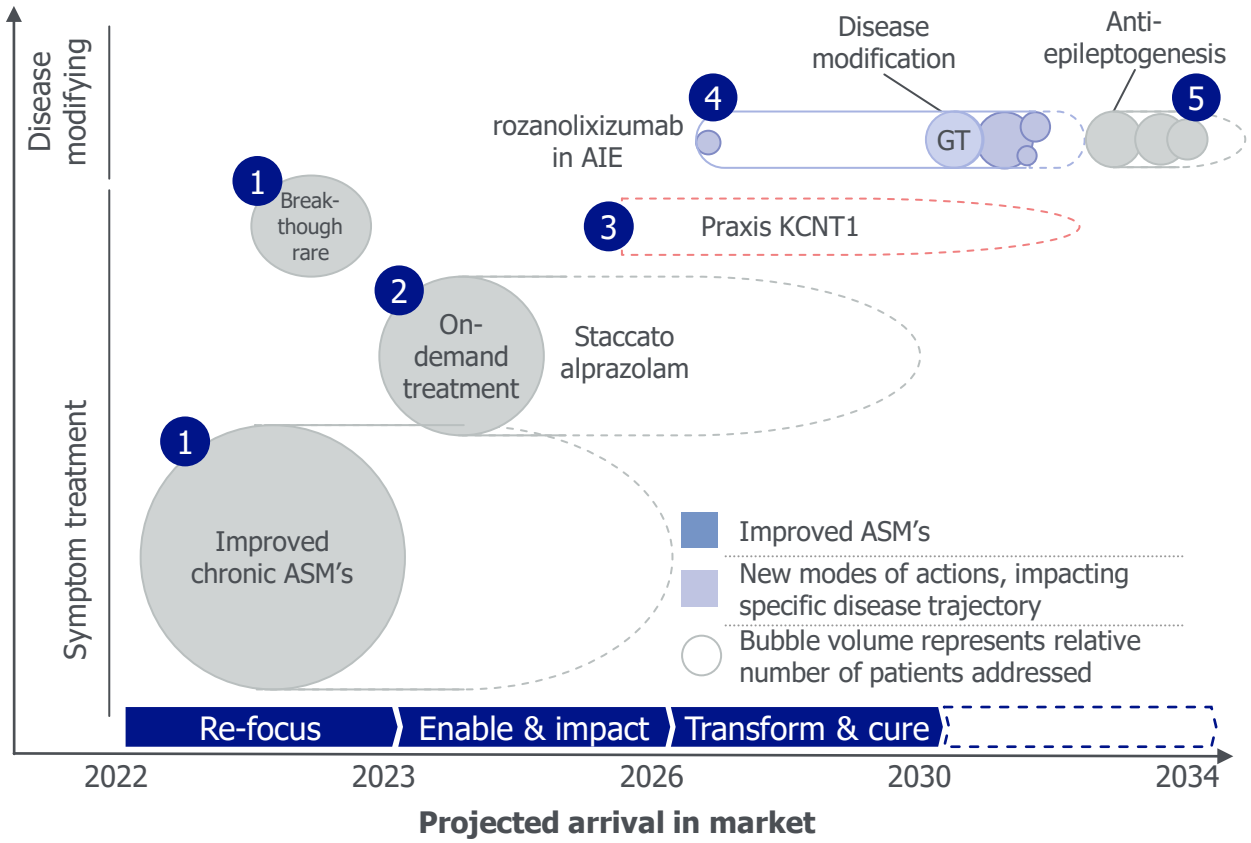
2 + 3 **Disease State Understanding + Pathobiology / Translational Medicine**

4 **TOMORROW**
More Targeted Therapies for Disease State Modification

Epilepsy Innovation Strategy

Focused on Five Value Pools

Projected arrival in market of innovation focus areas



1. **Improved chronic ASM's**
   - Optimize current portfolio through new formulations, indications and geographic expansion
   - Rare epilepsies: superior improvements in seizure frequency, comorbidities, and survival for DEE's with FFA
2. **On-demand treatment**
   - Rapid cessation of prolonged seizure events within 2 mins
   - Leverage STAP as entry and explore to combine with seizure sensors
3. **Innovation pre-disease modification**
   - Accelerating disease-targeting pipeline through inorganic growth opportunities
   - Introduce first non-ASM Tx targeting disease denominator
4. **Disease modification**
   - Targeting underlying pathological cause of the epilepsy impacting disease trajectory
5. **Anti-epileptogenesis**
   - Therapies for prevention of epilepsy disease (e.g. in case of trauma induced epilepsy)

AIE= autoimmune epilepsy, ASM= anti-seizure medication, DEE's = developmental epileptic encephalopathies, FFA = fenfluramine, GT = gene therapy, STAP = Staccato alprazolam, KCNT1= Potassium channel subfamily T, member 1

FINTEPLA®▼ (fenfluramine oral solution) Provides a New Set of Answers in Rare Epilepsy Syndromes

Konrad Werhahn, MD PhD
Epileptologist & Head of Global Epilepsy Medical Affairs, UCB

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Licenses and approved indications for Fintepla® vary by country.

Fintepla® Important Safety Information

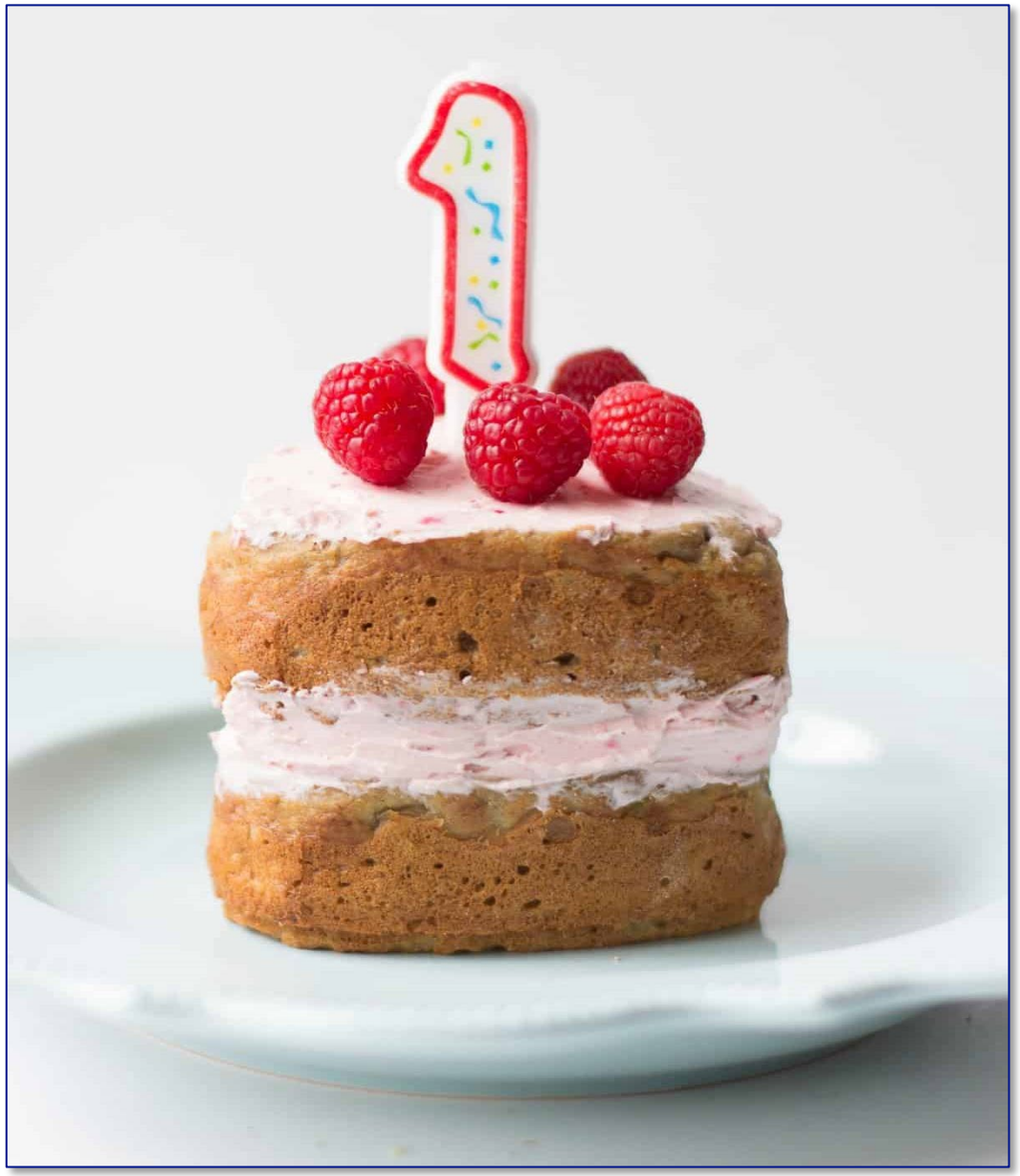
VALVULAR HEART DISEASE and PULMONARY ARTERIAL HYPERTENSION

There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension. Echocardiogram assessments are required before, during, and after treatment with Fintepla®.

Summary of safety profile

The most commonly reported adverse reactions are decreased appetite, diarrhoea, pyrexia, fatigue, upper respiratory tract infection, lethargy, somnolence, and bronchitis.

Please see additional important safety information at: www.finteplahcp.com



“A parent’s worst nightmare”

Developmental and epileptic encephalopathies: a group of rare, severe and complex epilepsies

- Typically occur in the **infancy and early childhood**
- High frequency of **drug resistant seizures**
- Associated with significant **intellectual, behavioural, physical and developmental delays**
- High **risk of premature death** due to sudden unexpected death in epilepsy (SUDEP), fatal status epilepticus, and accidents
- **Limited treatment options**

Dravet C, Epilepsia 2011;52 (S2):3–9; Raga et al., Epileptic Disord. 2021;23(1):40-52

Fenfluramine: What is the Value of a Unique and Dual MoA?

Antiseizure effects

Anti-seizure effects mediated by multiple serotonergic receptors and sigma (σ) pathway activity

- 5-HT_{1D}, 5-HT_{2A}, 5-HT_{2C} receptors[1,2]
- Positive modulator of σ1 receptor[2,3]

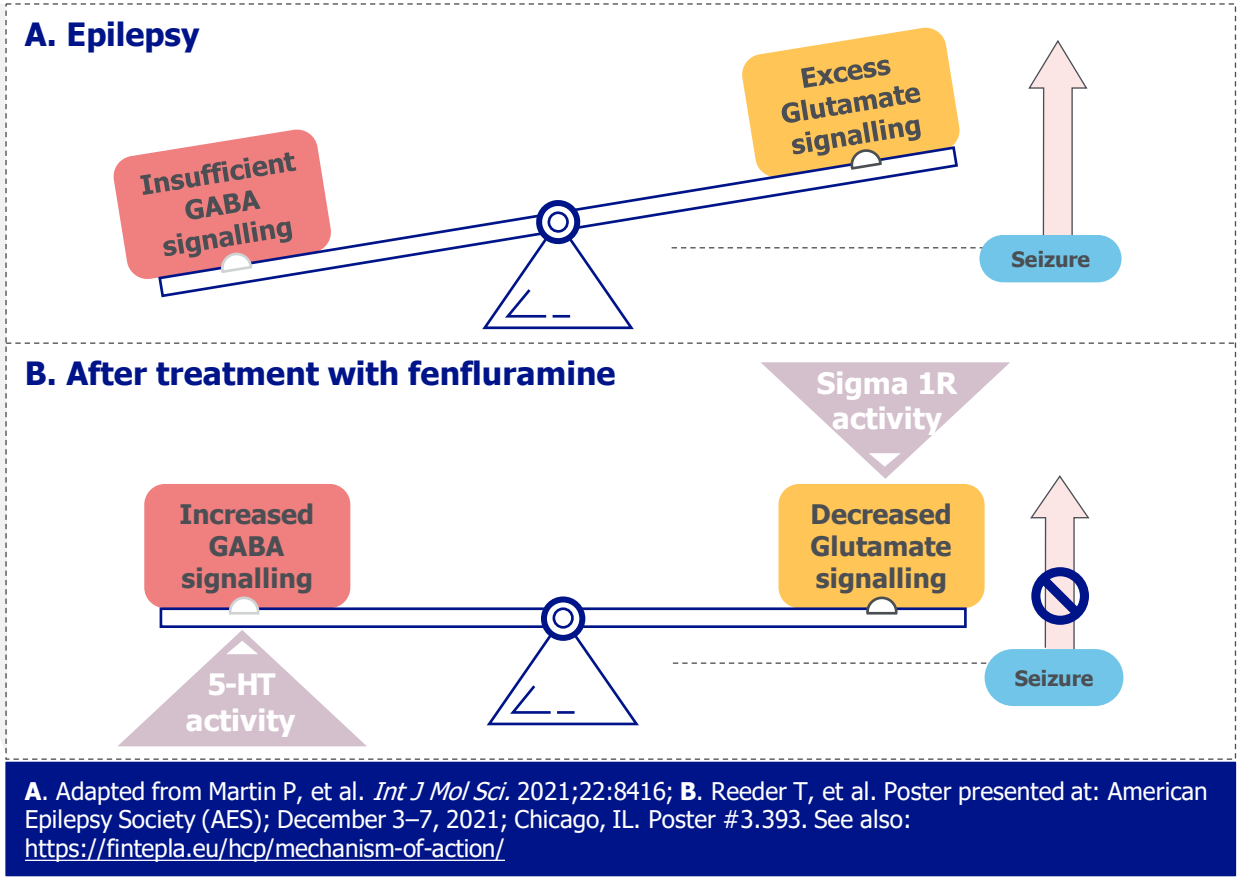
Nonseizure effects

Improved memory and cognition via serotonergic and σ pathways

- 5-HT_4 agonists demonstrated pro-cognitive effects in both animal and human models[4-6]
- Activity at σ1 receptors in mouse models[3]

SUDEP effects

Blocks seizure-induced respiratory arrest in a SUDEP mouse model via 5-HT_4 agonist activity[7]



A. Adapted from Martin P, et al. *Int J Mol Sci*. 2021;22:8416; **B**. Reeder T, et al. Poster presented at: American Epilepsy Society (AES); December 3–7, 2021; Chicago, IL. Poster #3.393. See also: https://fintepla.eu/hcp/mechanism-of-action/

5-HT, 5-hydroxytryptamine; FFA, fenfluramine; GABA, gamma aminobutyric acid; SUDEP, sudden unexpected death in epilepsy.
Fenfluramine is indicated for the treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older.

1. Sourbron J, et al. *Front Pharmacol*. 2017;8:191. 2. Rodríguez-Muñoz M, et al. *Oncotarget.* 2018;9:23373–23389. 3. Martin P, et al. *Epilepsy Behav*. 2020;105:106989. 4. Lamirault L, Simon H. *Neuropharmacology*. 2001;41:844–853; 5. Hagena H, et al. *Neurobiol Learn Mem*. 2017;138:145–153; 6. Murphy SE, et al. *Psychol Med.* 2020;50:2722–2730. 7. Tupal S, et al. *Epilepsy Res*. 2021;177:106777.

Fenfluramine Offers New Hope for Individuals and Families Living with Challenging Developmental Epileptic Encephalopathies (DEEs)

Dravet Syndrome (DS)	Lennox-Gastaut Syndrome (LGS)	CDKL5 Deficiency Disorder (CDD)
~12k-15k US, EU, JPN prevalence	**~60k-100k** US, EU, JPN prevalence	**~8k-10k** US, EU, JPN prevalence
>80% of patients remain uncontrolled on existing AED regimens Premature childhood mortality, primarily SUDEP, of **~20%**	Vast majority of patients on multi-drug treatment regimens of **2-5** ASMs as they experience multiple types of seizures, that change in type and frequency throughout life Higher risk of status epilepticus and sudden death	Nearly three-quarters of individuals with CDD take 2 or more ASMs simultaneously **>70%** of patients experience daily seizures High risk of SUDEP
Foundational Therapy *Profound impact on seizures exceeding expectations of what could be possible in DS*	**The New Next Option** *Proven efficacy on LGS's most challenging seizures proven efficacy as an adjunctive therapy*	**Phase 3 trial ongoing, topline results H2 2024** *Novel, complementary MOA with demonstrated impact on refractory seizure disorders*

ASM, Antiseizure medications; CDKL5, Cyclin-dependent kinase-like 5; MOA, Mode of action; SUDEP: sudden unexpected death in epilepsy
Specchio et al., 2022, Epilepsia; Zuberi et al., 2022, Epilepsia. Licenses and approved indications for Fintepla® vary by country.

Fenfluramine Creating Meaningful Value to Patients & HCPs across Dravet & Lennox-Gastaut Syndrome

Dravet Syndrome

Largest reduction in seizures associated with Dravet Syndrome – 1st or 2nd line recommendation in International DS Consensus.[14]

Dramatically lowers seizures leading to SUDEP mortality compared to previous standard of care – All-cause and SUDEP mortality rate was 1.7 per 1000 person-years compared to 9.3 related to SUDEP alone for persons with DS receiving standard-of-care.[4]

Improved everyday executive functioning Children and young adults who experienced a significant (≥50%) reduction of seizure frequency (78%) also showed improvement in emotional and cognitive regulation.[6]

Lennox-Gastaut Syndrome

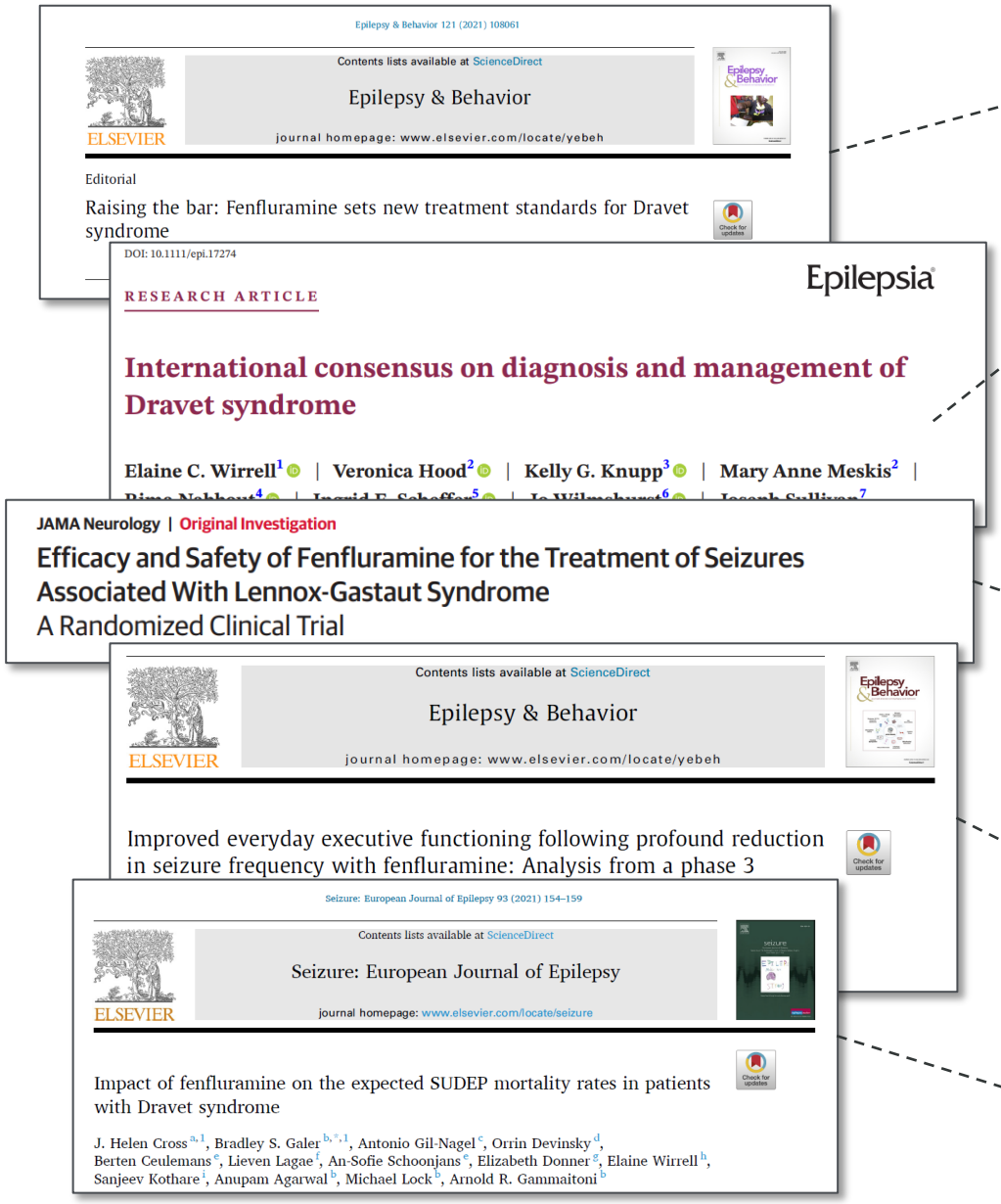
Profound seizure reduction in highest refractory population studied sustained for up to 15 months in added to current standard of care.[4,13]

Substantial improvement in LGS-related cognitive and functional deficits – emotion, behavior, cognition and QoL.[15]

Significant improvement in tonic-clonic seizures a primary risk factor for SUDEP.[12,13]

1. Sourbron J et al. Front Pharmacol 2017;8:191; **2**. Baumann MH et al. Neuropsychopharmacology 2014;39:1355–65; **3**. Fenfluramine Summary of Product Characteristics (SmPC); **4**. Knupp KG et al. Epilepsia. 2022;00:1–13; **5**. Martin P et al. Epilepsy & Behavior. 127 (2022) 108526; **6**. Bishop KI et al. Epilepsy & Behavior 121 (2021) 108024; **7**. Bishop K et al. American Academy of Neurology (AAN); April 17–22 2021; **8**. Lagae L et al. Lancet 2020;394:2243–54; **9**. Nabbout R et al. JAMA Neurol 2020;77:300–08; **10**. Sullivan J et al. Epilepsia 2020;61:2396–2404; **11**. Lai W et al. Epilepsia 2020;61:2386–95; **12**. Cross JH et al. Seizure 2021;39:154–159; **13**. Knupp et al. JAMA Neurol. 2022;79(6):554-564; **14**. Wirrell et al. Epilepsia 2022; 63(7):1761-1777; **15**. Jensen MP Epilepsy Research 185 (2022) 106976; **16**. Strzelczyk et al. Epilepsia. 2021; 62(10):2518-2527; **17**. Specchio N Epilepsia 2020;61(11):2405-2414.

Fenfluramine – In Their Words



"**Fenfluramine has raised the bar** for evaluating the efficacy of future therapies in Dravet syndrome, both for seizures and for critically important patient-centered outcomes "[2]

"For the first time, it became possible for a large percentage of patients to achieve **profound reductions in convulsive seizure frequency**"[3]

Generalized tonic-clonic seizures are commonly observed in patients with LGS. **The magnitude of response was similar to the reduction observed in patients with DS.**

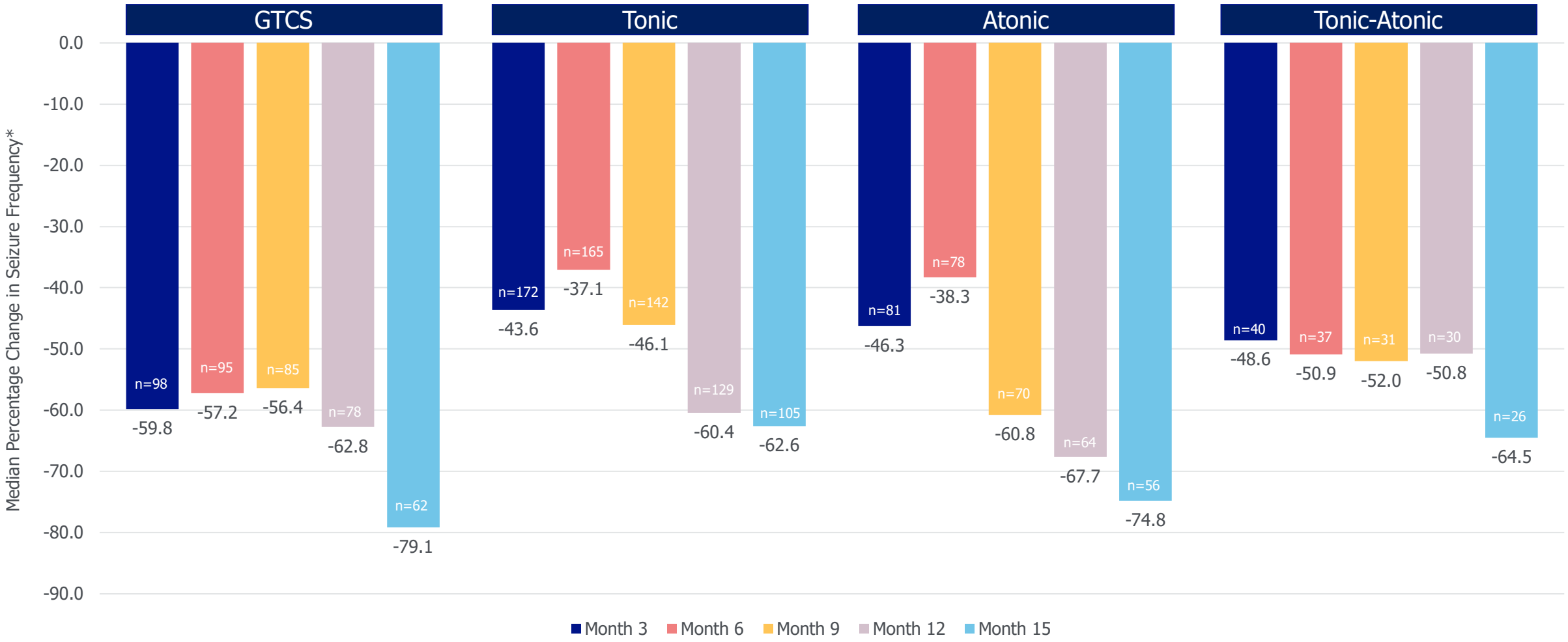
"Improved everyday executive functioning following profound reduction in seizure frequency with fenfluramine"[4]

"DS patients treated with FFA experienced **a substantially lower rate of all-cause and SUDEP-related mortality** compared with a historical natural history cohort"[1]

NNT=Number Needed to Treat. BRIEF, Behavior Rating Inventory of Executive Function; DS, Dravet syndrome; FFA, fenfluramine, MCSF, monthly convulsive seizure frequency; PAH, pulmonary arterial hypertension; VHD, valvular heart disease; [1]Cross et al., Seizure 2021 Dec;93:154-159: [2]Sullivan and Cross. Epilepsy Behavior 2021 Aug;121(Pt A):108061; [3]Wirrell et al. Epilepsia 2022; 63(7):1761-1777; [4]Bishop KI et al. Epilepsy & Behavior 121 (2021) 108024

Fenfluramine Open-Label Extension (LGS)

Frequency Reduction by Seizure Subtype (based on N=247 patients entering Open-Label Extension study)



Knupp KG et al. Epilepsia 2022 Oct 5. doi: 10.1111/epi.17431. Online ahead of print. Data source: NCT03355209; LGS, Lennox-Gastaut Syndrome, GCTS, generalized tonic–clonic seizures;
* versus randomized clinical trial baseline

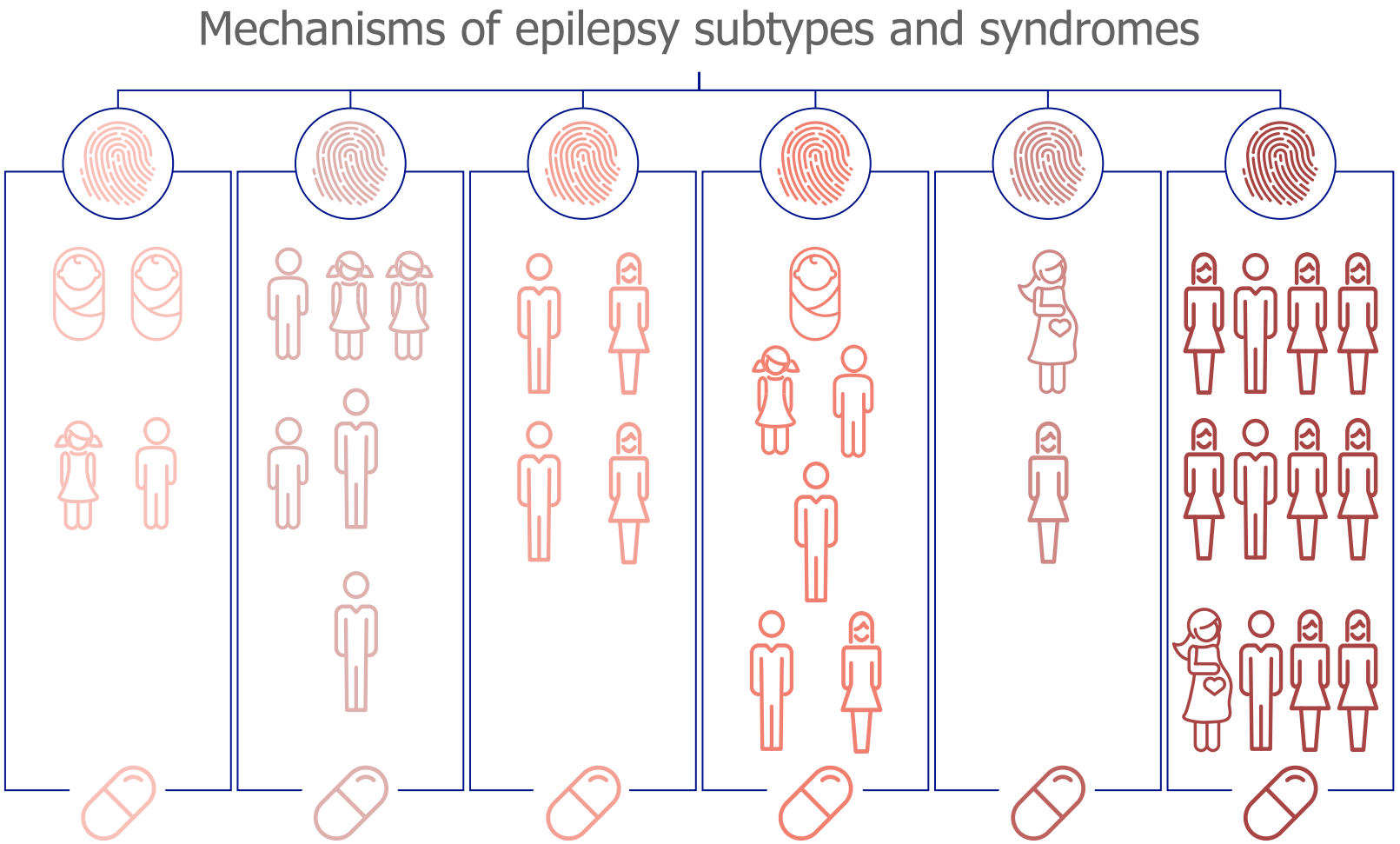
Early Solutions Leveraging Novel Science and Human Pathobiology for Improved Drug Targeting in Epilepsy

Stefanie Dedeurwaerdere, PhD
Head of Epilepsy Discovery, UCB

Inspired by patients.
Driven by science.

How Could Treatments Become more Personalized?

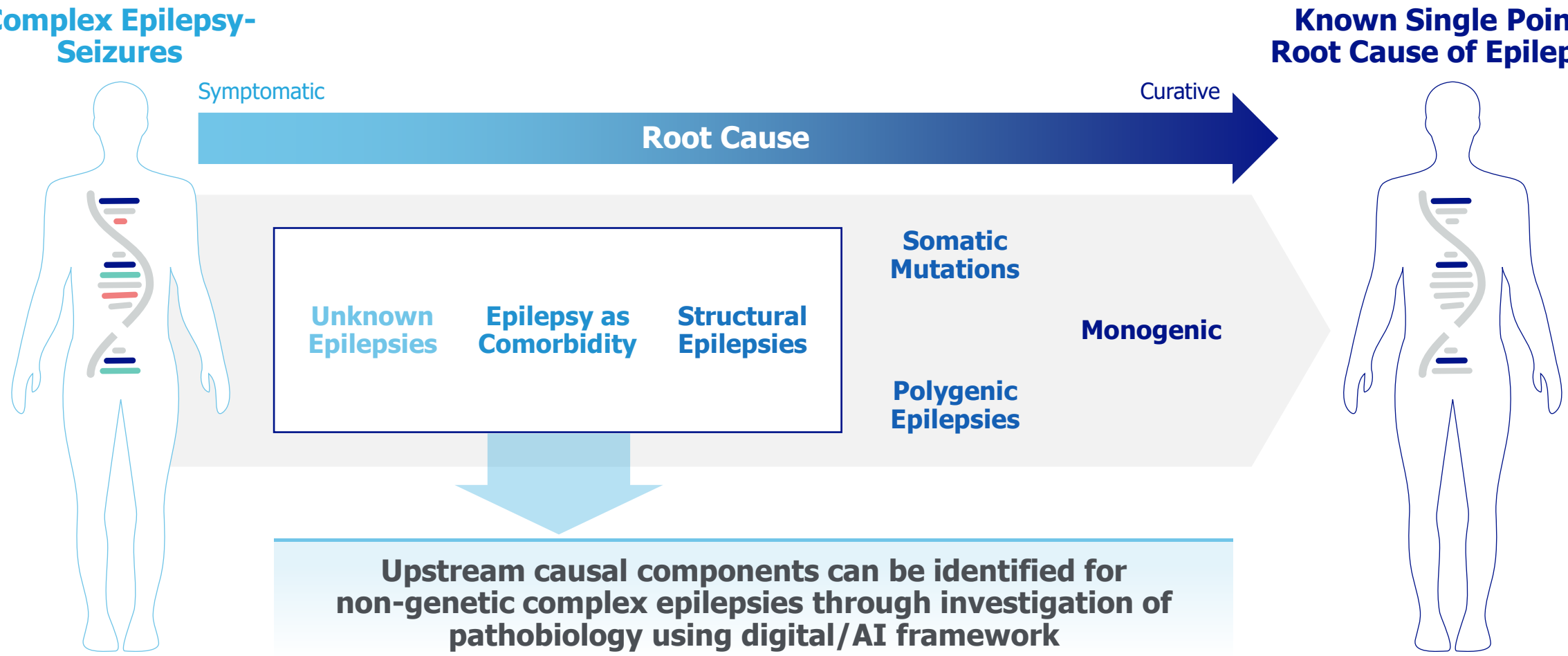
How to Develop Treatments Tailored to Disease Mechanisms and Pathobiology?



In many patients, seizures are still not well controlled!

In many patients, seizures are not the only symptom!

Molecular Taxonomy – Focus on Etiology & Entry Points for Molecularly Targeted Treatments

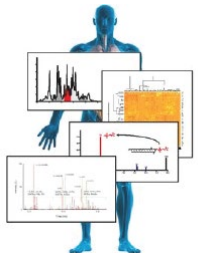


UCB R&D Leveraging Human Pathobiology and Digital AI Framework in Epilepsy

UCB R&D Epilepsy Engine

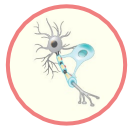
mRNA profiling of epilepsy samples

mTLE TSC
FCD IIa GG
FCD IIb DNT



Library of mRNA Epilepsy Big Data

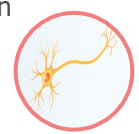
Disease characterization



Neuronal support and myelination

Brain extracellular matrix

Epilepsy



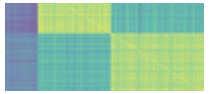
Neuronal function

Energy metabolism

Neuroinflammation and immune response

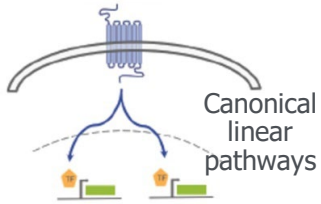
Identification of disease regulatory mechanism

Epilepsy



Profiling Analysis

Understanding of Pathways & Downstream targets



Canonical linear pathways

Biological knowledge-relevance of disease models for transactional hypothesis

Epilepsy platforms (Glia, CRISPR technology)

Target assessment & prioritization

Disease

Drugs

Text mining

Therapeutic Landscape

Genes

Gene expression

Pathways

UCB's Differentiation*

R&D = research and development, mTLE=mesial temporal lobe epilepsy, TSC=tuberous sclerosis complex, FCD=focal cortical dysplasia, GG=ganglioglioma, DNT=developmental neuroepithelial tumor, CRISPR=clusters of regularly interspaced short palindromic repeats; *UCB internal assessment

Scientific Advances Combined with Digital Pathobiology are Driving Discovery Pipeline

Patient segmentation is based on a number of criteria…

The targeted population has to be **identifiable** based on underlying pathobiology

The **unmet need** in the targeted population has to be large and the gain for patients high.

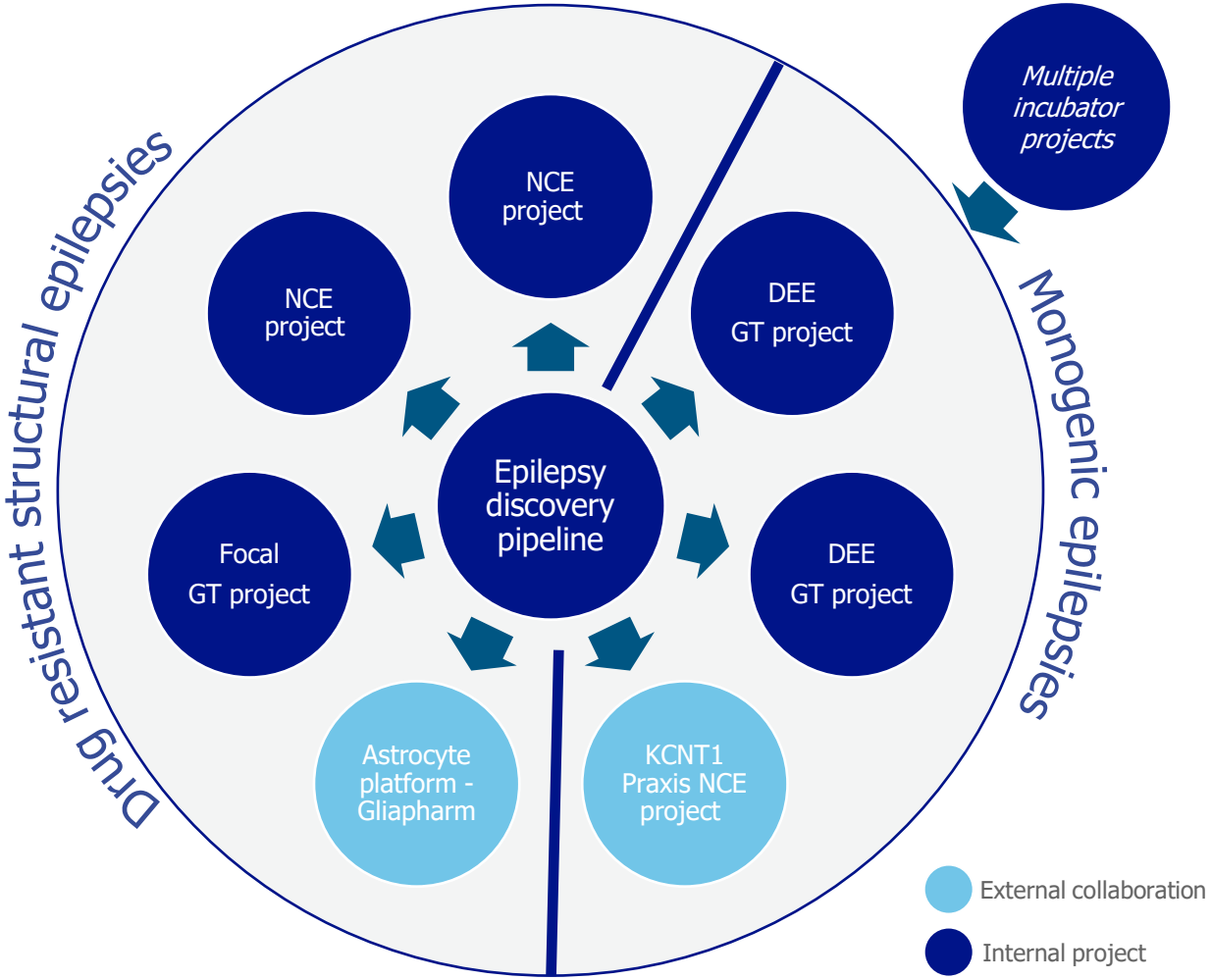
Aside

Monogenic diseases are of interest as they can be targeted at the root cause by **gene therapy and NCEs**

…and driven by **scientific advances** in the field

Scientific maturity
Potential for innovation
UCB enabling discovery platforms
Competitive edge

Multiple Incubator projects
Several discovery pipeline assets including small molecule and gene therapy modalities

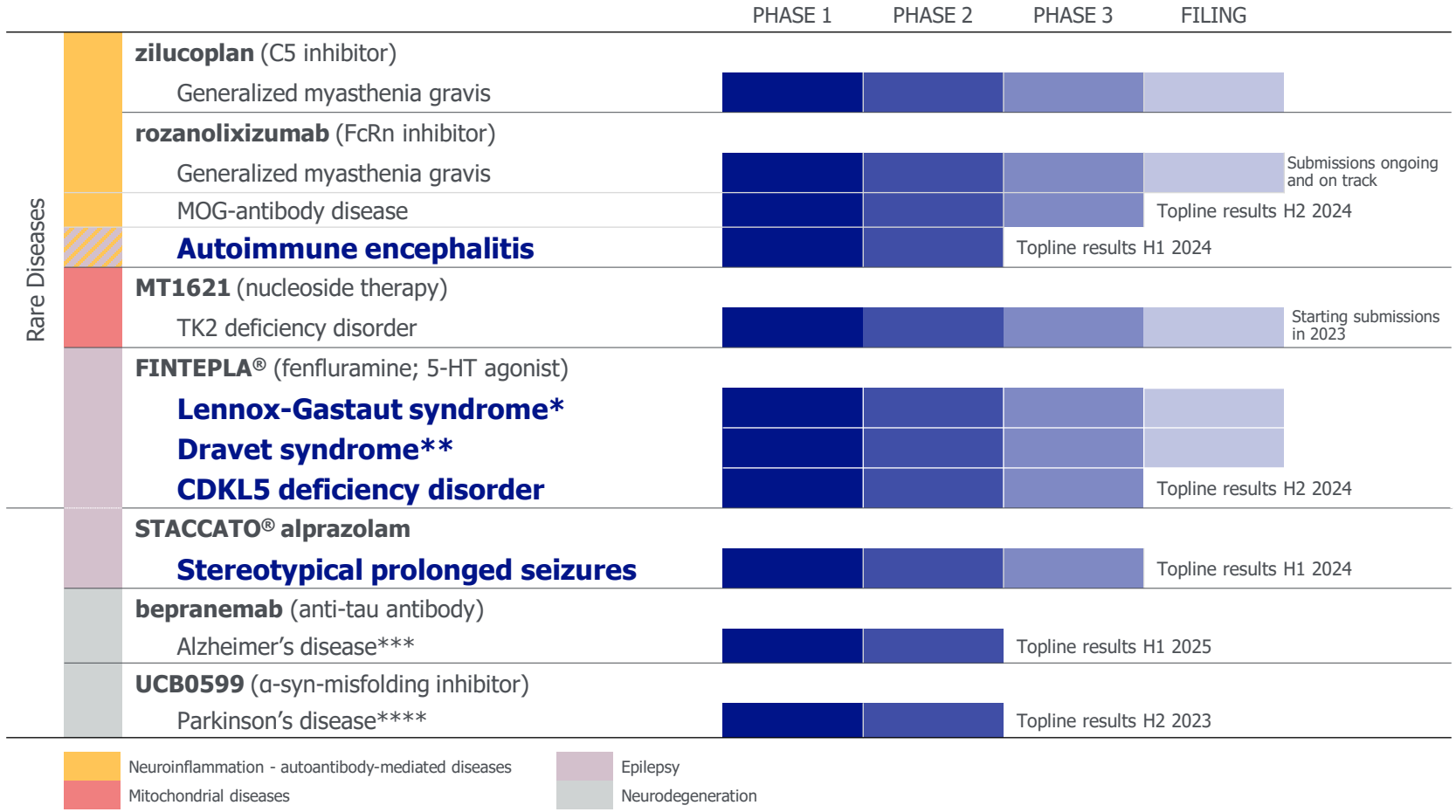


NCE, new chemical entity; GT, gene therapy; DEE, Developmental and Epileptic Encephalopathy, KCNT1, Potassium channel subfamily T, member 1

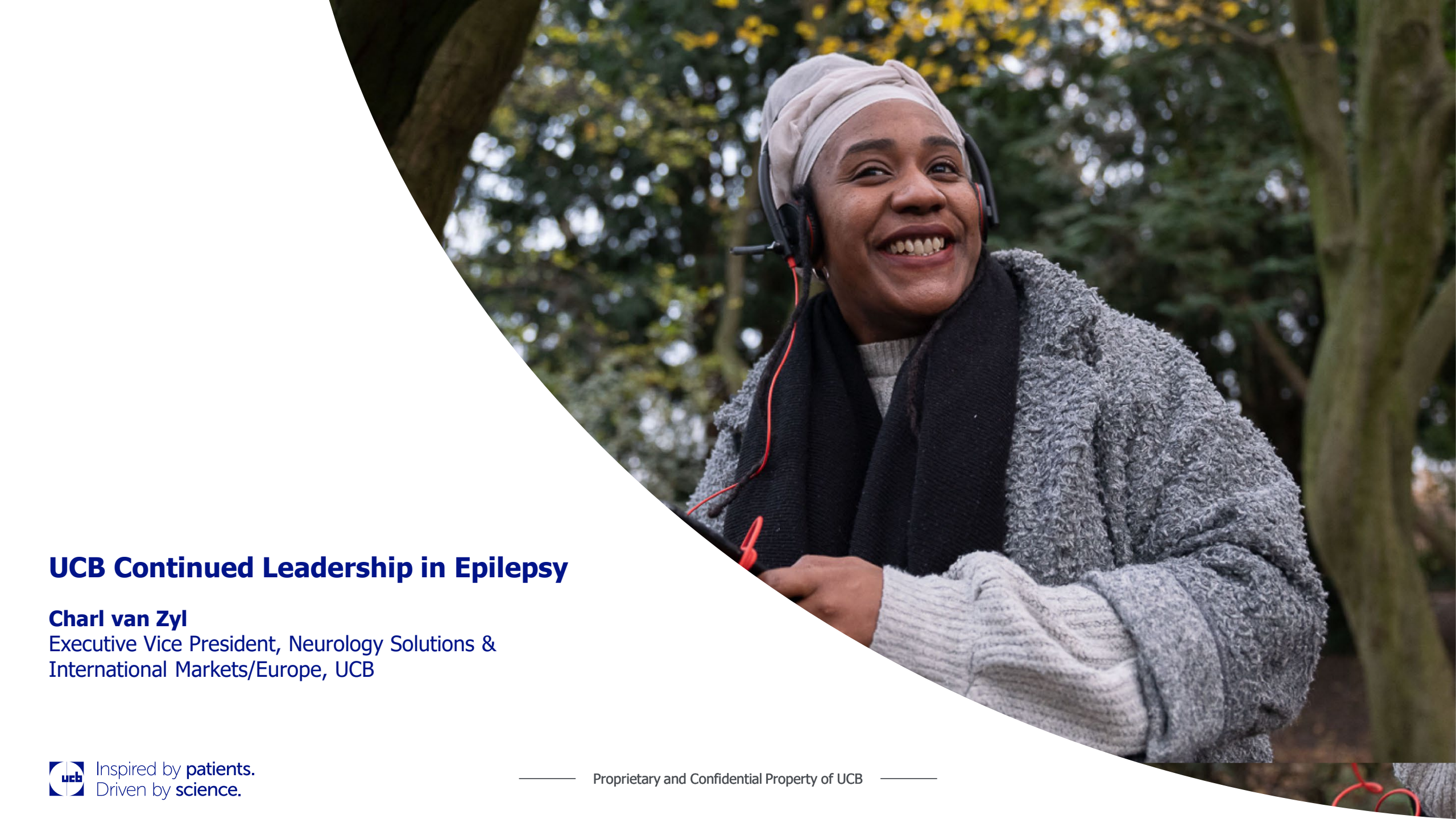
UCB Late-Stage Pipeline in Neurology

Addressing Unmet Medical Needs and Bringing Clinically-Meaningful Improvements to People Living with Epilepsy and Neuroinflammatory & Neurodegenerative Diseases

Active Epilepsy Incubator and Early Discovery Pipeline
(multiple Incubator projects and several discovery pipeline assets including small molecule and gene therapy modalities)



*Launched in US; submitted in EU + other geographies; **Launched in US and EU; approved in Japan; submitted in other geographies; ***in partnership with Roche/Genentech; ****in partnership with Novartis; 5-HT - 5-hydroxytryptamin or serotonin; α-syn – alpha-synuclein; C5 – complement component 5; CDKL5 - cyclin-dependent kinase-like 5; H – half-year; FcRn - Neonatal fragment crystallizable receptor; MOG - myelin oligodendrocyte glycoprotein; Q – quarter; SUDEP - sudden unexpected death in Epilepsy; TK2d - thymidine kinase 2 deficiency



UCB Continued Leadership in Epilepsy

Charl van Zyl
Executive Vice President, Neurology Solutions &
International Markets/Europe, UCB

The Evolution of UCB's Epilepsy Pipeline into Precision Medicine with the Continued Ambition for Curative Therapy

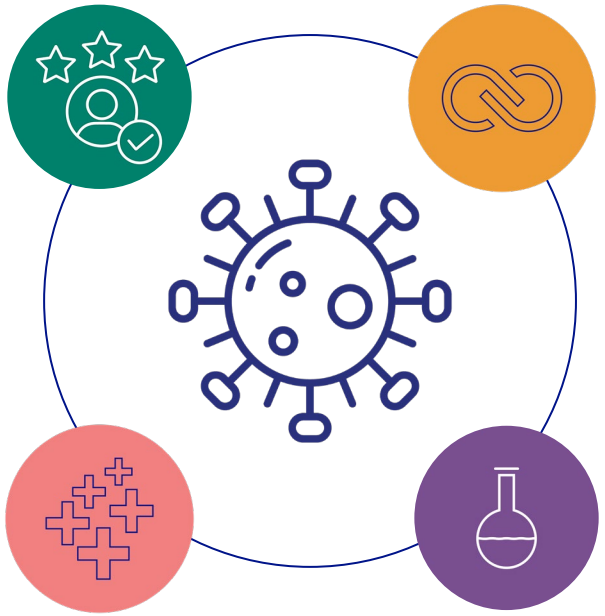
Digitized End-to-End Model (Patient-centric Business) - from Discovery to Patients

Commitment to Patients, Research and Education

- Move from molecules aimed to increase the suppression of seizures to targeting pathobiology
- Expansion into causal components of epilepsies with greatest unmet needs

Precision Medicine

- Developing drugs to modulate the pathways identified
- Greater specificity at molecular level allows for expansion into personalized therapies



Translational Medicine

- Ensuring transfer of the science based on pathobiology to loadable clinical endpoints and value for patients

Drug Discovery

- Identify targets and candidate therapies that modulate critical pathways responsible for causal components of epilepsy

UCB Leading in Epilepsy

Epilepsy remains a core pillar of UCB's strategy to bring differentiated value to patients

Elevating care for the patient populations we serve

Innovating science for symptom suppression, disease modification and cure

Leading the wider ecosystem

Q&A

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Thank you

Inspired by patients.
Driven by science.