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Company Presentation

SVB Leerink CNS Day

June 29, 2021

Forward-Looking Statements

Zogenix cautions you that statements included in this press release that are not a description of historical facts are forward-looking statements. Words such as “believes,” “anticipates,” “plans,” “expects,” “indicates,” “will,” “intends,” “potential,” “suggests,” “assuming,” “designed,” and similar expressions are intended to identify forward-looking statements. These statements include timing of commercial launch of FINTEPLA for the treatment of Dravet syndrome in additional countries in Europe, including France; Zogenix’s expectations on the submission of a J-NDA by Nippon Shinyaku in Japan; the timing and ability of Zogenix to complete regulatory submissions in the United States and the European Union for FINTEPLA in LGS; Zogenix’s plans to expand FINTEPLA in other indications including the timing or success of a Phase 3 clinical trial in CDKL5 deficiency disorder and investigator-initiated clinical trials in other indications; Zogenix’s belief that the recent Type B meeting with the FDA supports an NDA submission for MT1621 in TK2 deficiency and the timing of such submission. These statements are based on Zogenix’s current beliefs and expectations. The inclusion of forward-looking statements should not be regarded as a representation by Zogenix that any of its plans will be achieved. Actual results may differ from those set forth in this release due to the risks and uncertainties inherent in Zogenix’s business, including, without limitation: Zogenix may not be successful in executing its sales and marketing strategy for the commercialization of FINTEPLA in the U.S. and Europe, including due to the costs and procedures related to the REMS certification process or controlled access program; the COVID-19 pandemic may disrupt Zogenix’s business operations, impairing the ability to commercialize FINTEPLA and may delay Zogenix’s development plans for FINTEPLA and MT1621; unexpected adverse side effects or inadequate therapeutic efficacy of FINTEPLA or MT1621 that could limit development or commercialization, or that could result in recalls or product liability claims; additional data from Zogenix’s ongoing studies may contradict or undermine the data previously reported; and other risks described in Zogenix’s prior press releases as well as in public periodic filings with the U.S. Securities & Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Zogenix undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.

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Zogenix Pipeline

Committed to Transforming the Lives of Families Living with Rare Disease

Project & Indication	Preclinical	Phase 1	Phase 2	Phase 3	Regulatory	Commercialization

Rare, Treatment-Resistant Epilepsies

Fintepla®

(fenfluramine) oral solution

- **Dravet Syndrome – United States** — *FDA Approved*
- **Dravet Syndrome – Europe** — *MAA Approved*
- **Dravet Syndrome – Japan** — *Positive Phase 3 Trial*
- **Lennox-Gastaut Syndrome** — *Positive Phase 3 Trial*
- **CDKL5 Deficiency Disorder** — *Phase 3 Trial*
- **Other Rare Epilepsies** — *Investigator Initiated Trials*

Thymidine Kinase 2 Deficiency (TK2d)

MT1621

Substrate enhancement therapy

- **TK2d** — *Positive Efficacy Trial*

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Market Opportunities

Dravet Syndrome	Lennox Gastaut Syndrome	CDKL5 Deficiency Disorder	TK2d Deficiency
~12k-15k US, EU, JPN prevalence	**~60k-100k** US, EU, JPN prevalence	**~8-10k** US, EU, JPN prevalence	**~1-2k** US, EU, JPN prevalence
>80% of patients remain uncontrolled on existing AED regimens Premature childhood mortality, primarily SUDEP, of **~20%**	Typical childhood onset (2-7 yrs.) with varied disease etiology Vast majority of patients on multi-drug treatment regimens of **2-5** AEDs	Disease onset at birth, continues throughout life **>70%** of patients experience daily seizures Currently **0** approved therapies	**~50%** of patients are infantile onset, with life expectancy of 1-3 years Profound loss/impairment of mobility, respiratory, eating, other functions **0** approved therapies
Fintepla®			MT-1621
Unprecedented sustained seizure reduction	First-in-class mechanism; highly effective reduction in severe, convulsive seizures	Initial open-label efficacy in convulsive seizures similar to results seen in Dravet	Potential transformational, disease-modifying therapy
>$1B Opportunity			**>$300M Opportunity**

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MT-1621 | TK2 Deficiency

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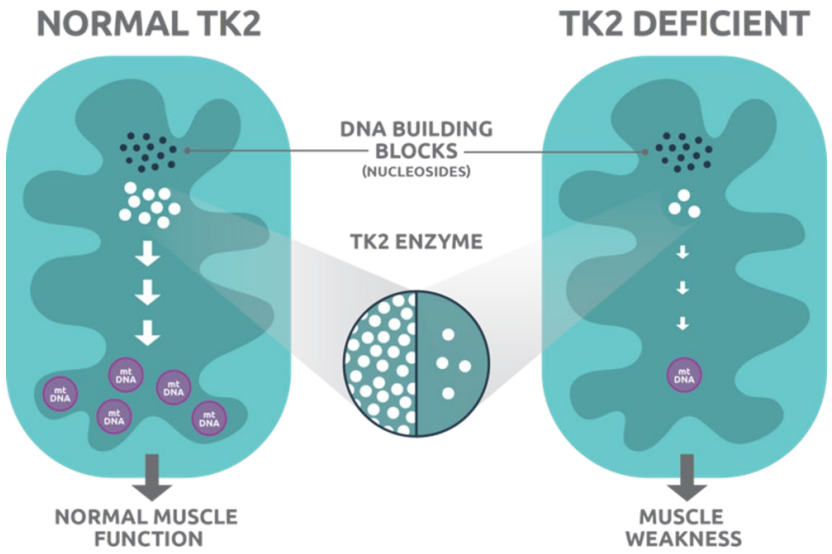
Thymidine kinase 2 (TK2) deficiency

Rare, genetic, progressive and often fatal mitochondrial DNA depletion syndrome

- Autosomal recessive mutations in TK2 gene
- First patient described in 2001
- Clinically characterized by severe muscle weakness, profoundly impairing movement, breathing, eating/nutrition, and other normal functions
- Untreated patients show progressive decline which is often fatal. No spontaneous recovery has been reported
- Age of onset is prognostic for outcome; younger patients have high mortality
- TK2d impacts 1K-2K patients in the US, Europe, and Japan
- Currently no approved therapies; treatment limited to supportive care



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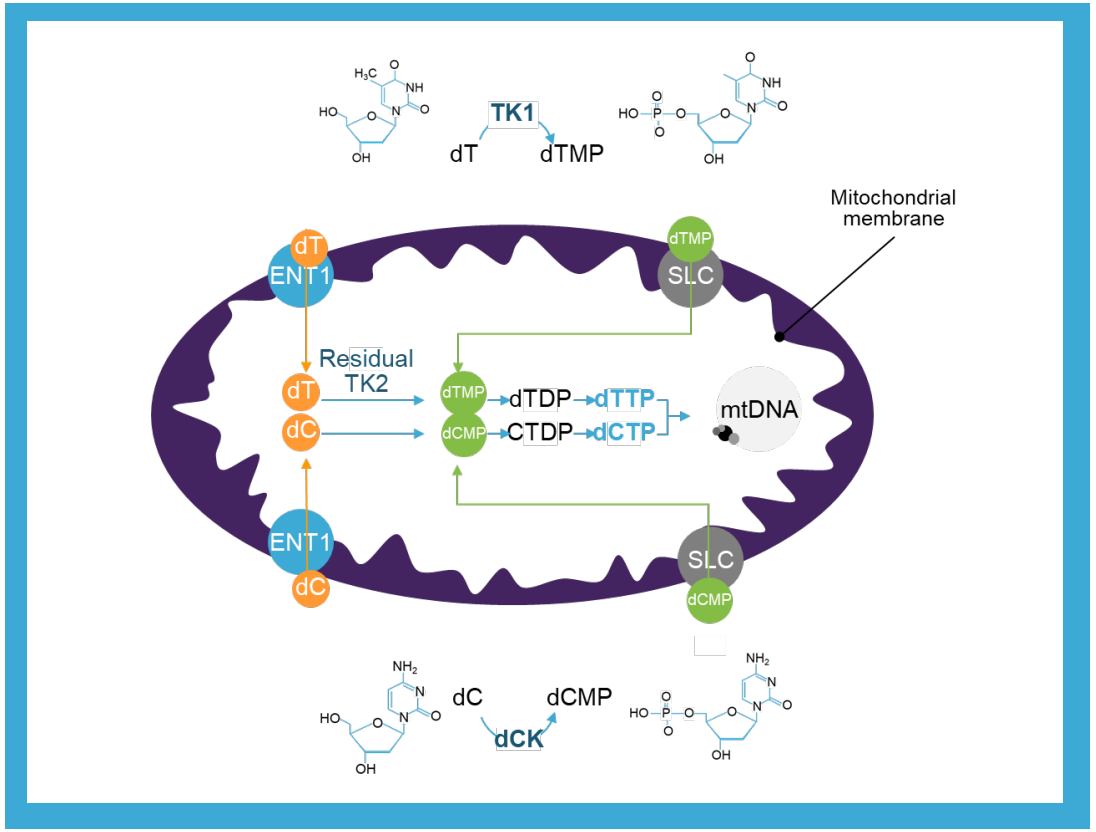
Substrate Enhancement Therapy to Restore Mitochondrial Function

MT1621 is an orally administered investigational deoxynucleoside combination therapy for TK2 deficiency

- TK2 phosphorylates deoxycytidine (dC) and deoxythymidine (dT), fundamental building blocks in production of mitochondrial DNA (mtDNA)
- MT-1621 (dC/dT) utilizes alternative enzyme phosphorylation pathways and any residual TK2 activity to restore mitochondrial function
- Deoxynucleoside combination therapy improved nucleotide balance, increased mtDNA copy number, improved cell function, and prolonged life in preclinical models of TK2d
- Breakthrough Therapy Designation in the US and PRIME designation in Europe



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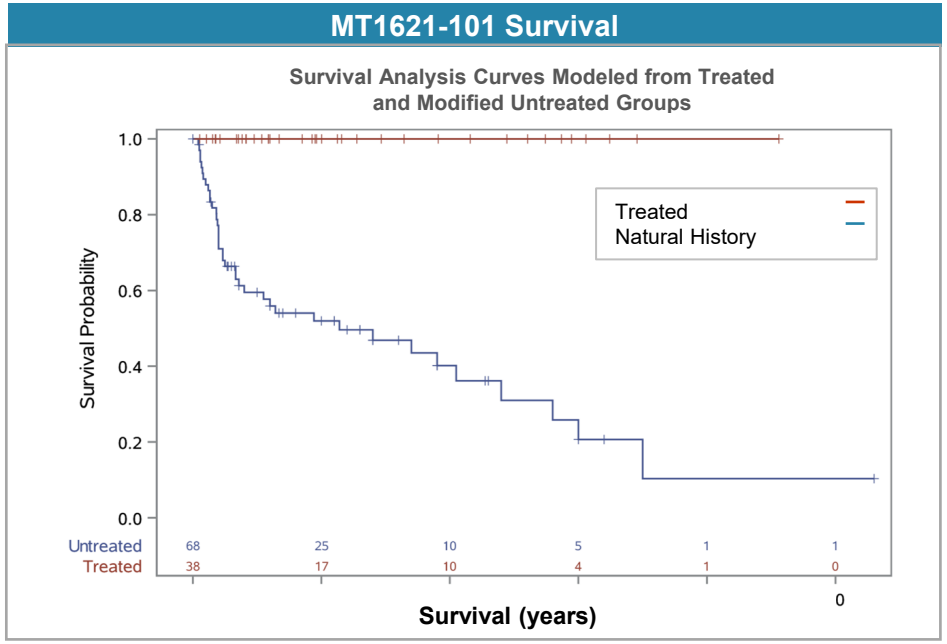
Key Results from "RETRO" Study MT1621-101

- ✓ **Comprehensive**: survival, milestones, functional measures, respiratory endpoints, feeding/growth
- ✓ **Longitudinal**: encompasses untreated (pre-) → treated (post-treatment) course
- ✓ **Representative**: spectrum of TK2d patients (all ages of onset; disease severities)
- ✓ **Treatment duration:** ranging from 3 months to nearly 7 years



Survival analysis comparing treated patients in RETRO study with untreated patients (TK2d Natural History data set) showed statistically significant effect of pyrimidine nucleosides on survival ($p<0.004$)

Age of Onset Category	Number of Deaths/Total Number of Patients	
	Untreated Patient Dataset (UPD)	Treated Patients in Study MT-1621-101
≤ 2 Years of Age	46/63 (73%)	0/15 (0%)
> 2 to ≤ 12 Years of Age	2/19 (10.5%)	0/14 (0%)
> 12 Years of Age	8/16 (50%)	0/9 (0%)
Overall	58/103 (56.3%)	0/38 (0%)

All treated patients surviving!

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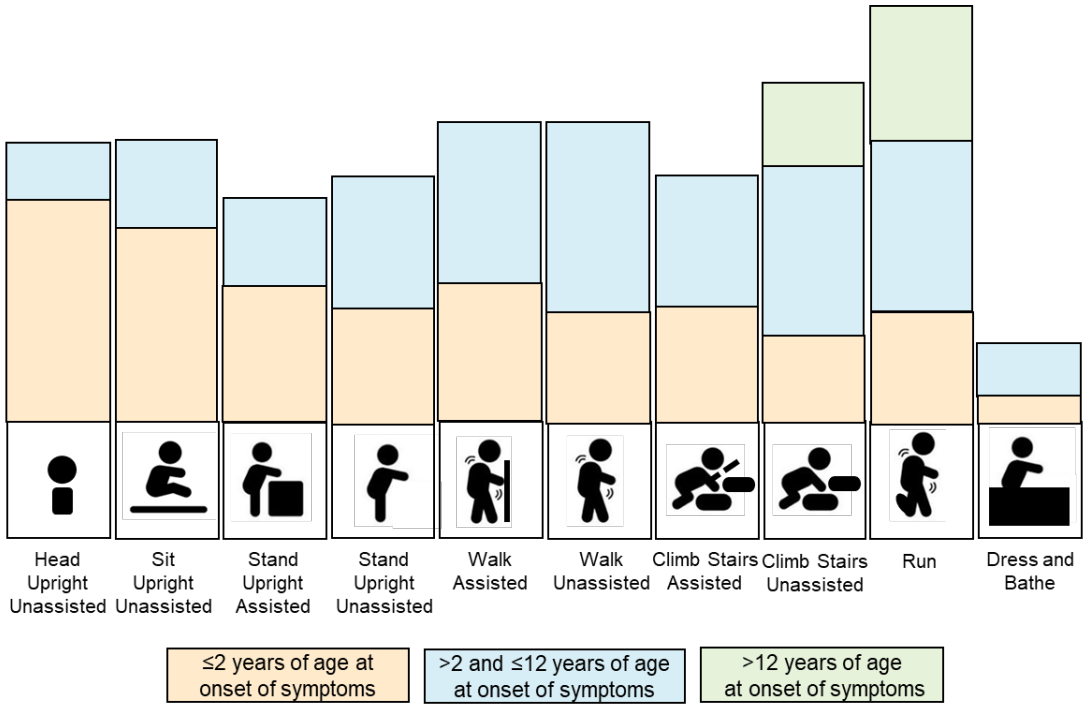
Study MT1621-101 Efficacy on Major Motor Milestones

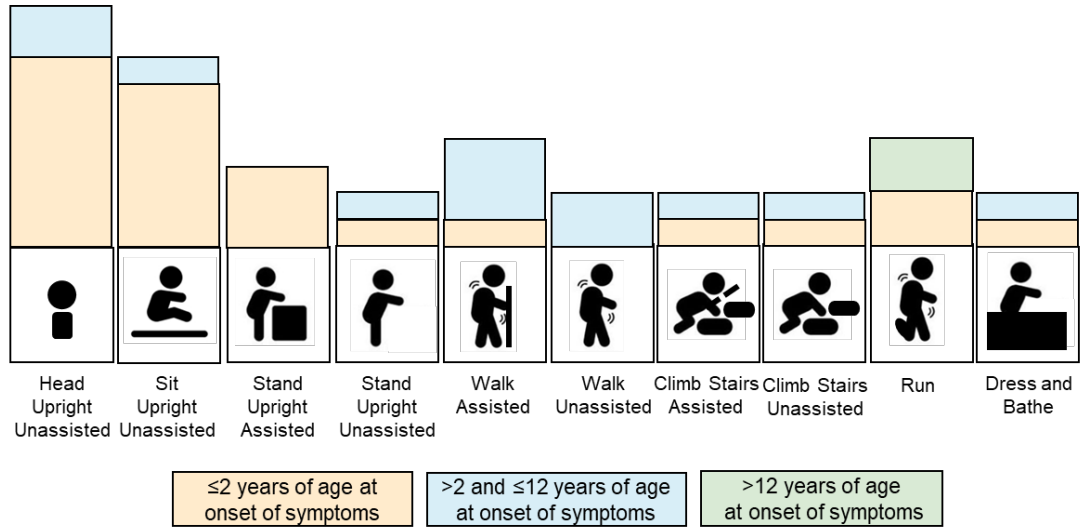
Pre-Treatment *Loss* of Motor Milestones

25 of 38 patients (66%) lost motor milestones



Post Treatment *Regain* of Motor Milestones

17 of 25 patients (68%) regained motor milestones



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Study MT1621-101 Non-Survival Treatment Benefits

Ambulation

3 patients who had lost ability to walk prior to treatment, regained ambulation on treatment; 1 who had never walked gained ambulation

Respiratory

1 patient on 24-hour ventilation support prior to treatment was able to discontinue all ventilation support

Feeding

8 patients were on feeding tubes prior to treatment; 3 were able to remove feeding tubes after treatment

Motor milestones and Functional scales (Hammersmith Functional Motor Scale, 6-minute walk test, Northstar Ambulatory Assessment, Egen Klassifikation)

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MT1621 Current Clinical Program

Study	Description	N	Status
TK2 DEFICIENCY STUDIES			
NA	Untreated Patient Dataset *(*literature)	103	Ongoing
MT1621-101	Ph 2 RETROspective study	38	Completed
MT1621-102	Ph 2 Prospective, open-label continuation study	47*	Ongoing
MT1621-107	Ph 2 Retrospective chart review study to collect vital status of untreated and treated patients	TBD	Ongoing
CLINICAL PHARMACOLOGY STUDIES			
MT1621-103	PK and food effect (healthy volunteers)	14	Completed
MT1621-105	PK and food effect (healthy volunteers)	14	Completed
MT1621-106	Renal Impairment Study	32	Dosing complete

*includes 35 pts who were in Study 101+ 12 addl pts;

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MT1621 Regulatory Strategy

- Per FDA guidance, a single adequate, well controlled clinical investigation and confirmatory evidence may be sufficient to establish effectiveness
- Factors for consideration /persuasiveness of single trial; robustness of confirmatory evidence; seriousness of disease (unmet need); size of patient population; ethics and practicality of conducting more than one trial

Basis of Nulibry[1] (fosdenopterin) approval Feb 2021	Relevance for MT1621

• Adequate, well controlled clinical investigation based on survival analysis of treated patients pooled from 2 prospective, single-arm studies and 1 retrospective study vs. a retrospective and prospective Natural History study **(n=37)**
• Confirmatory evidence: mouse and biomarker data
• Chemically equivalent forms of drug (recombinant and synthetic forms) included in filing package
	• Reliance on retrospective and prospective studies and natural history
	• Survival comparison vs. external control group
	• Confirmatory evidence
	  • mouse model data (survival benefit),
	  • mechanistic data (mtDNA incorporation)
	  • additional clinical data (treated and untreated patients)
	• Studies include chemical-grade and MT1621 (GMP)

(1) Indicated to reduce risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A

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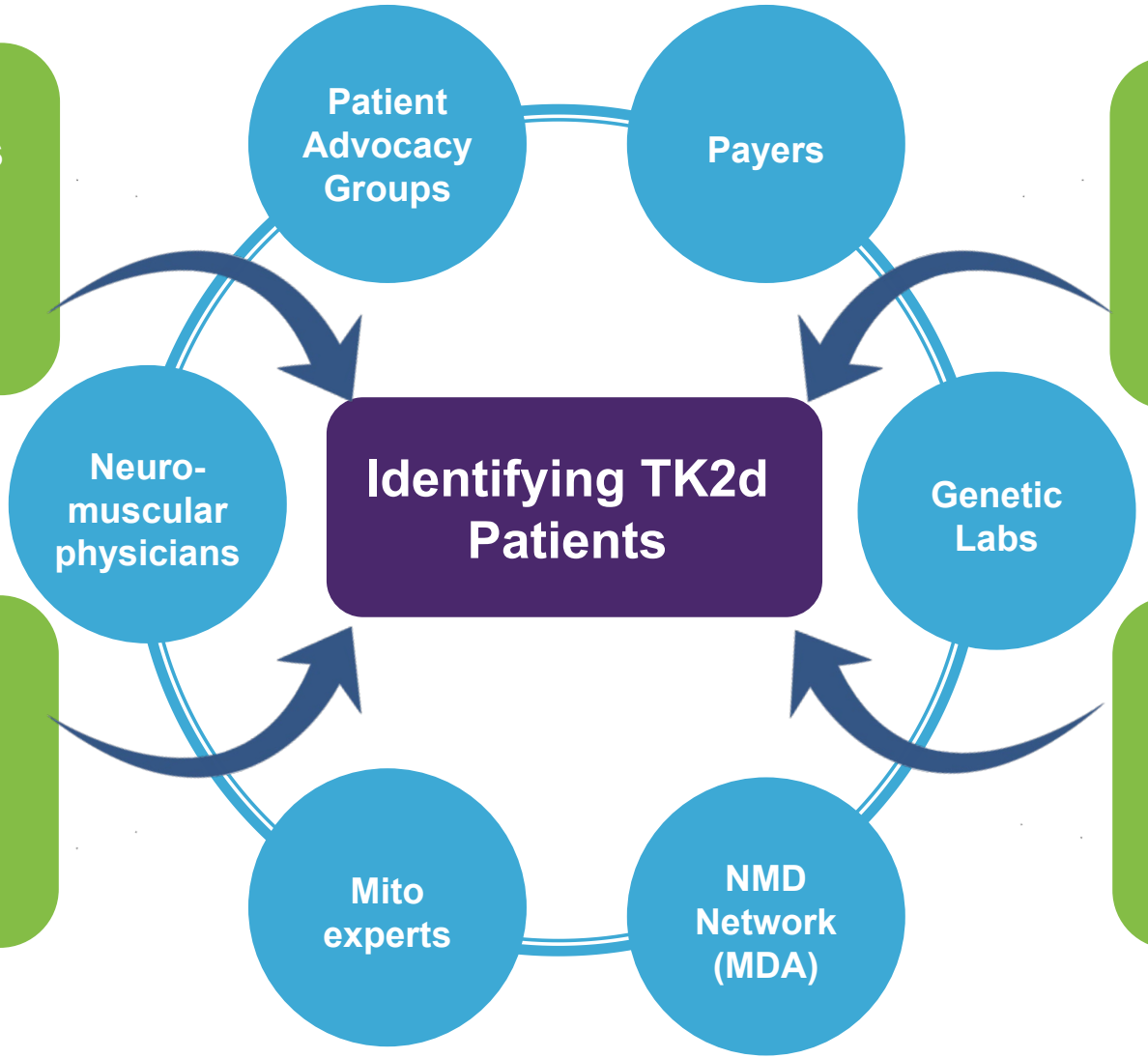
Collaborations with TK2d Community to find patients

Mito/TK2d disease and genetic test awareness

- Raise clinical suspicion
- Drive urgency for genetic test

Define Diagnostic Algorithm

- Clarity on criteria, tests, steps
- Focus on genetic test



Lab Partnerships

- Ensure TK2d on lab panels
- Reduce access barriers, e.g., no cost test program

Pilot Programs

- HCP Directed
- Patient/Community Directed

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MT-1621 Exclusivity

Patents

- Exclusive license to Method of Treatment of TK2 Deficiency Disorder, other MDDS*
  - **US10471087 Issued Expiry: 08/07/2036**
  - Counterparts issued in Europe, Japan, Australia
- Composition and Method of Use IP
  - US20210054014 Pending
- Additional applications filed

Regulatory

- New Chemical Entity and Orphan Drug exclusivities
- Hatch-Waxman § 156 patent extensions
- Deoxycytidine and deoxythymidine are excluded from the category of "dietary supplement" that can legally be sold to the public (DSHE Act, Pub. L. 103–396, Oct. 1994)

*Mitochondrial DNA Depletion Syndromes

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Zogenix Upcoming Milestones

Fintepla®

MT-1621

	Dravet syndrome	Lennox-Gastaut syndrome	CDKL5 Deficiency Disorder (CDD)	TK2 Deficiency
Q1 2021	Commercial launch in Europe (Germany) ✓			
Q2 2021				
Q3 2021	Commercial launches in additional EU countries	sNDA submission in U.S.		
Q4 2021	J-NDA submission in Japan	MAA submission in Europe Study 1601 Japan top-line results	First patient enrolled in global Phase 3 study	All clinical, non-clinical and CMC data available for NDA and MAA submissions
2022	Marketing approval in Japan	Marketing approval U.S. Marketing approval Europe J-NDA submission in Japan		NDA submission in U.S. MAA submission in Europe

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