Important Notice

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: the potential for Zogenix’s product candidates to provide new treatment options. 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: FINTEPLA may not achieve broad market acceptance as a treatment option of Dravet syndrome which would limit Zogenix’s ability to general revenues; 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 continue to disrupt Zogenix’s business operations, impairing the ability to commercialize FINTEPLA in Europe and Zogenix's ability to generate product revenue in Europe and conduct its development programs; unexpected adverse side effects or inadequate therapeutic efficacy of fenfluramine that could limit regulatory approval or commercialization, or that could result in recalls or product liability claims; later developments with FDA that may be inconsistent with the already completed meetings; additional data from Zogenix's ongoing studies may contradict or undermine the data previously reported; the potential for the FDA to delay timing of review of the sNDA due to the FDA's internal resource constraints or other reasons; 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.
About Zogenix

A global pharmaceutical company focused on serious rare diseases

• **Fintepla®** (fenfluramine) lead product approved in the U.S. and Europe for the treatment of Dravet syndrome and under development for the treatment of seizures associated with rare, catastrophic, difficult-to-treat epilepsies

• **MT1621** product candidate in late-stage development for TK2d, a rare, often fatal mitochondrial deficiency disease

• Headquarters in the San Francisco Bay Area

• Additional operations in Europe; partnerships in Japan & Israel

• ~300 employees

• ~$343m cash and marketable securities on September 30, 2021
# Zogenix Pipeline

Committed to transforming the lives of patients and families living with rare disease

<table>
<thead>
<tr>
<th>Project &amp; Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Regulatory</th>
<th>Commercialization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rare, Treatment-Resistant Epilepsies</strong></td>
<td></td>
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<tr>
<td>Dravet Syndrome</td>
<td>FDA &amp; MAA Approved, Japan P3 complete</td>
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<tr>
<td>Lennox-Gastaut Syndrome (LGS)</td>
<td><a href="#">sNDA and MAA Type 2 Variation submitted</a></td>
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<tr>
<td>CDKL5 Deficiency Disorder (CDD)</td>
<td><img src="#" alt="Investigator Initiated Trials" /></td>
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<tr>
<td>Other Rare Epilepsies</td>
<td><img src="#" alt="Investigator Initiated Trials" /></td>
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<tr>
<td><strong>Mitochondrial Depletion Syndromes (MDS)</strong></td>
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<tr>
<td><strong>MT1621</strong></td>
<td><img src="#" alt="Positive Efficacy Trial" /></td>
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<tr>
<td>Substrate enhancement therapy</td>
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<tr>
<td><strong>Other Substrate Enhancement Therapies</strong></td>
<td><img src="#" alt="MDS" /></td>
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<tr>
<td><strong>tRNA based therapies</strong></td>
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<td><img src="#" alt="MT1621" /></td>
<td><img src="#" alt="MT1621" /></td>
<td><img src="#" alt="MT1621" /></td>
<td><img src="#" alt="MT1621" /></td>
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</table>
# Market Opportunities

<table>
<thead>
<tr>
<th>Dravet Syndrome</th>
<th>Lennox Gastaut Syndrome</th>
<th>CDKL5 Deficiency Disorder</th>
<th>TK2d Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>~12k-15k</td>
<td>~60k-100k</td>
<td>~8k-10k</td>
<td>~1-2k</td>
</tr>
<tr>
<td>US, EU, JPN prevalence</td>
<td>US, EU, JPN prevalence</td>
<td>US, EU, JPN prevalence</td>
<td>US, EU, JPN prevalence</td>
</tr>
</tbody>
</table>

- **Dravet Syndrome**
  - >80% of patients remain uncontrolled on existing AED regimens
  - Vast majority of patients on multi-drug treatment regimens of 2-5 AEDs
  - Unprecedented sustained seizure reduction
  - >80% of patients remain uncontrolled on existing AED regimens
  - Premature childhood mortality, primarily SUDEP, of ~20%

- **Lennox Gastaut Syndrome**
  - Typical childhood onset (2-7 yrs.) with varied disease etiology
  - Initial open-label efficacy in convulsive seizures similar to results seen in Dravet
  - First-in-class mechanism; highly effective reduction in severe, convulsive seizures

- **CDKL5 Deficiency Disorder**
  - Disease onset at birth, continues throughout life
  - >70% of patients experience daily seizures
  - Currently 0 approved therapies

- **TK2d Deficiency**
  - Disease onset at birth, continues throughout life
  - >70% of patients experience daily seizures
  - Currently 0 approved therapies

- **MT-1621**
  - Potential transformational, disease-modifying therapy

- **>$1B Opportunity**
- **>$300M Opportunity**
Fintepla®

Dravet Syndrome
Lennox-Gastaut Syndrome
CDKL5 Deficiency Disorder
Additional Rare, Treatment-Resistant Epilepsies
Fintepla® (ZX008, fenfluramine oral solution)

- FDA and EMA approved in 2020 for the treatment of seizures associated with Dravet syndrome in patients 2 year of age and older
- Launched in U.S. and Germany and cATU authorization in France
- Three positive global pivotal global Phase 3 trials completed
- Primary endpoint and all key secondary endpoints met with high statistical significance
- Ongoing OLE has shown robust efficacy results up to three years

Dravet Syndrome

- Positive pivotal global Phase 3 trial completed
- Top-line results announced Q1 2020
- Primary endpoint met with high statistical significance at 0.7 mg/kg dose; several key secondary endpoints met with statistical significance
  - sNDA and MAA under review, PDUFA date of March 25, 2022

Lennox-Gastaut Syndrome

- Phase 3 efficacy study in CDKL5 deficiency disorder in Q1 2022

CDKL5 Deficiency Disorder, Other Epilepsies

- Other treatment-resistant epilepsies e.g., Doose syndrome, sunflower syndrome, etc. through investigator-initiated studies
Dravet Syndrome

A rare and frequently catastrophic epilepsy

Affects 1/15,700 live births in the U.S. (about 200-250 infants/year)

Highly treatment resistant
  - 72% of patients take 3 or more antiepileptic drugs
  - >80% of patients are inadequately controlled on traditional antiepileptic treatment regimens

Significant morbidity
  - High seizure frequency; significant developmental and motor impairments

Increased risk of death
  - 6x-higher risk of death, most commonly due to SUDEP (sudden unexpected death in epilepsy) and Status Epilepticus
  - 46% of caregivers use pulse-ox at night due to fear of death from SUDEP

Urgent need to reduce or eliminate high seizure burden and associated comorbidities

Dravet Syndrome Phase 3 Trial Efficacy Results

Primary Endpoint Analysis of % Difference From Placebo in Reduction in Mean Monthly Convulsive Seizures

**Study 1**
- 0.7 mg/kg/day: 70.0% (p<0.001)
- 0.2 mg/kg/day: 31.7% (p=0.043)

**Study 2**
- 0.4 mg/kg/day: 59.5% (p<0.001)

**Notes**
- p-value compared to placebo
- Source: Fintepla prescribing information
- 1. All 0.4 mg/kg/day patients were also taking concomitant stiripentol, which increases the exposure of Fintepla.
Dravet Syndrome Study 1503 Open Label Extension Study

Robust seizure reduction sustained in OLE at up to three years with no evidence of waning therapeutic effect

Reduction in Median Mean Convulsive Seizure Frequency (MCSF) Over Time During Fenfluramine Treatment in Open Label Extension (OLE) Study

Median Treatment Duration: 631 days (7-1086)

Median Reduction in MCSF: -83%, P=0.002

The decrease in patient number is primarily due to staggering study entry and not due to patient withdrawal.

Data originally presented at AAN 2021
Safety Highlights in Dravet Syndrome

Fintepla is only available through the Fintepla REMS Program

- Fintepla is available only through a restricted distribution program called the Fintepla REMS because of the risk of valvular heart disease and pulmonary arterial hypertension.

Boxed Warning: 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 (ECHO) assessments are required before, during, and after treatment with Fintepla.

Contraindications

- Fintepla is contraindicated in patients with hypersensitivity to fenfluramine or any of the excipients in Fintepla and with concomitant use of, or with 14 days of, the administration of monoamine oxidase inhibitors because of an increased risk of serotonin syndrome.

No patient has developed valvular heart disease or pulmonary arterial hypertension in controlled or uncontrolled studies of up to 3 years in duration.

*Please see full Prescribing Information for additional Important Safety Information and a complete list of the adverse events reported to date
Fintepla Commercialization

HCP, caregiver awareness; integrated support from enrollment through continued use

**Clinical Education**
- Clinician and caregiver education about unmet medical needs and Fintepla® clinical data

**Zogenix Central Hub**
- Integrated support programs and specialty pharmacy distribution

**Long-Term Support**
- Dedicated case management to ensure proper monitoring and education

U.S. & Europe: Zogenix in-house commercial teams

Japan: Commercial partner Nippon Shinyaku Co. Ltd.
Lennox-Gastaut Syndrome

Rare, highly refractory, and notoriously difficult to treat

- Childhood onset, usually between 2-7 years of age
- Varied disease etiology
- Significant intellectual, behavioral, and motor disabilities
- Higher risk of status epilepticus and sudden death
- Most patients’ seizures remain uncontrolled on current antiepileptic treatment regimens
- Accounts for ~1-4 % of all cases of childhood epilepsy¹
- 60,000-100,000 living with LGS in the U.S. and Europe combined²

Patients require constant care, creating high physical, emotional, and financial burden for caregivers and the entire family

2. Zogenix company estimates
LGS Phase 3 Study 1601 Primary Efficacy Endpoint

Primary endpoint met demonstrating Fintepla, at a dose of 0.7 mg/kg/day, was superior to placebo as adjunctive therapy in the treatment of LGS based on median percent change in monthly frequency of seizures that result in drops (p=0.0012)

Key secondary endpoint met: number of subjects with ≥50% reduction in drop seizures: Fintepla 0.7 mg/kg/day group compared to placebo

p-values are treatment compared with placebo
LGS Study 1601 Additional Efficacy Analyses

Subgroup Analysis by Seizure Types, Median Percentage Seizure Reduction From Baseline

**Generalized Tonic-Clonic (GTC) Seizures**

<table>
<thead>
<tr>
<th>Group</th>
<th>Median % Reduction From Baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7 mg/kg/day FFA</td>
<td>49.7</td>
<td>P=0.0007</td>
</tr>
<tr>
<td>0.2 mg/kg/day FFA</td>
<td>58.2</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Placebo</td>
<td>-3.7</td>
<td></td>
</tr>
</tbody>
</table>

**Tonic-Atonic Seizures**

<table>
<thead>
<tr>
<th>Group</th>
<th>Median % Reduction From Baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7 mg/kg/day FFA</td>
<td>46.7</td>
<td>P=0.0455</td>
</tr>
<tr>
<td>0.2 mg/kg/day FFA</td>
<td>13.7</td>
<td>NS</td>
</tr>
<tr>
<td>Placebo</td>
<td>6.8</td>
<td></td>
</tr>
</tbody>
</table>

Data originally presented at AAN 2021
Study 1601 Safety Results

- Generally well-tolerated with adverse events consistent with known safety profile of fenfluramine
- No cases of valvular heart disease or pulmonary arterial hypertension
- Six patients in the 0.7/mg/kg/d group had an AE that led to a discontinuation compared to four patients in the 0.2/mg/kg/d group and one patient in the placebo group
- One death during the trial caused by SUDEP in a patient in the 0.7/mg/kg/d group assessed to be unrelated to study drug

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=87)</th>
<th>0.2 mg/kg/d (n=89)</th>
<th>0.7 mg/kg/d (n=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects With at Least One Treatment Emergent Adverse Event (AE)</td>
<td>79.3%</td>
<td>76.4%</td>
<td>89.7%</td>
</tr>
<tr>
<td>Number of Subjects With at Least One Serious Treatment Emergent Adverse Event (SAE)</td>
<td>4.6%</td>
<td>4.5%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Most Common Adverse Events (&gt;10%)</td>
<td>Placebo (n=87)</td>
<td>0.2 mg/kg/d (n=89)</td>
<td>0.7 mg/kg/d (n=87)</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>13 (14.9%)</td>
<td>18 (20.2%)</td>
<td>32 (36.8%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (4.6%)</td>
<td>10 (11.2%)</td>
<td>11 (12.6%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (5.7%)</td>
<td>12 (13.5%)</td>
<td>9 (10.3%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>11 (12.6%)</td>
<td>8 (9.0%)</td>
<td>16 (18.4%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>11 (12.6%)</td>
<td>11 (12.4%)</td>
<td>9 (10.3%)</td>
</tr>
<tr>
<td>Seizure</td>
<td>5 (5.7%)</td>
<td>11 (12.4%)</td>
<td>5 (5.7%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>10 (11.5%)</td>
<td>10 (11.2%)</td>
<td>15 (17.2%)</td>
</tr>
</tbody>
</table>
# Fintepla Intellectual Property Position

## Patents and regulatory exclusivity protection

| Global Commercialization Rights | • Exclusive worldwide license  
| • Full data and patent rights in rare epileptic encephalopathies |

<table>
<thead>
<tr>
<th>Orphan Drug Exclusivity</th>
<th>U.S.</th>
<th>Europe</th>
<th>Japan</th>
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<tbody>
<tr>
<td>• Dravet: 7.5-year Orphan &amp; Pediatric Drug exclusivity</td>
<td>• Dravet: 12-year Orphan &amp; Pediatric Drug exclusivity</td>
<td>• Dravet: 10-year Orphan Drug exclusivity</td>
<td></td>
</tr>
<tr>
<td>• LGS: 7-year Orphan Drug exclusivity</td>
<td>• LGS: 10-year Orphan Drug exclusivity</td>
<td>• LGS: Seeking Orphan Drug exclusivity</td>
<td></td>
</tr>
</tbody>
</table>

| Strong Patent Portfolio | U.S. & International patents with expiries 2033-2039 |
| 8 Orange Book listed patents in the U.S.  
| Coverage for Dravet syndrome and other rare epileptic encephalopathies  
| Coverage for proprietary methods of manufacture (API), drug product formulation (pending), and Safety/REMs |
MT-1621: 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
- Currently no approved therapies; treatment limited to supportive care
MT-1621: dC/dT Substrate Enhancement Therapy

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
MT-1621: Key Results from Study 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

### Age of Onset Category

<table>
<thead>
<tr>
<th>Age of Onset Category</th>
<th>Modified Untreated Patient Dataset (MUPD) N=69</th>
<th>Treated Patients in Study MT-1621-101 N=38</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2 years, n (%)</td>
<td>31 / 40 (77.5%)</td>
<td>0 / 15 (0%)</td>
</tr>
<tr>
<td>&gt; 2 to ≤ 12 years, n (%)</td>
<td>2 / 16 (12.5%)</td>
<td>0 / 14 (0%)</td>
</tr>
<tr>
<td>&gt; 12 years, n (%)</td>
<td>7 / 13 (53.8%)</td>
<td>0 / 9 (0%)</td>
</tr>
<tr>
<td>Overall, n (%)</td>
<td>40 (58.0%)</td>
<td>0 / 38 (0%)</td>
</tr>
</tbody>
</table>
MT1621: Study 101 Efficacy on Major Motor Milestones

25 of 38 patients (66%) lost motor milestones

Post Treatment *Regain* of Motor Milestones
17 of 25 patients (68%) regained motor milestones
MT1621: Intellectual Property and 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
Key Financial Data

- $343mm Cash and Marketable Securities as of September 30, 2021
- $230mm in Convertible Senior Notes with 2.75% annual interest, due 2027
- $51.3mm of Net Product Sales of FINTEPLA for the nine months ended September 30, 2021
- Operating Expenses of $213.0mm\(^{(1)}\) for the nine months ended September 30, 2021:
  - R&D of $100.9mm
  - SG&A of $104.7mm
- 56.0mm common stock outstanding as of October 27, 2021\(^{(2)}\)

\(^{(1)}\) Includes $5.9mm amortization of intangible asset and change in fair value of contingent consideration of $1.5mm.

\(^{(2)}\) Excludes 6.6mm options outstanding at a weighted average exercise price of $26.58 and 0.8mm outstanding restricted stock units as of September 30, 2021 or 9.5mm shares reserved for issuance upon conversion of Convertible Senior Notes at initial conversion price of $24.28/share.
## Upcoming Milestones

<table>
<thead>
<tr>
<th>Q1 2022</th>
<th>Q2 2022</th>
<th>Q3 2022</th>
<th>Q4 2022</th>
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<tbody>
<tr>
<td>Dravet syndrome</td>
<td>Lennox-Gastaut syndrome</td>
<td>CDKL5 Deficiency Disorder (CDD)</td>
<td>TK2 Deficiency</td>
</tr>
<tr>
<td>Commercial launches in additional EU countries</td>
<td>U.S. Marketing Approval</td>
<td>First patient enrolled in global Phase 3 study</td>
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<tr>
<td>Japan Marketing Approval</td>
<td>Potential for CHMP feedback on E.U. LGS Type IIa variation</td>
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<td>U.S. NDA submission (2H 2021)</td>
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Together we can bring hope and support to patients and families impacted by rare diseases.