2023 Nano-rare Patient Colloquium

Stanley T. Crooke, Md, PhD
Founder, CEO and Chairman of the Board
THANK YOU

To Chris, Natacha, Sandra Yi-Fuller, Sandra Merisier, Corina Hadjiodyseos and her story telling team and all the wonderful people of Biogen
The Important Roles of Our Annual Nano-rare Patient Colloquium

- To share our aspirations with you
- To share our quality processes with you
- To share our progress with you
- To share all the important lessons, we are learning with you
- To listen to patients and families, investigators, patient advocacy groups and others
- To celebrate our successes
- To honor our pioneer patients
- To help create a strong, cohesive, empathetic and knowledgeable nano-rare community
- To enlist the support of every single person
- To give hope to the hopeless, by demonstrating that we are delivering help to many who were otherwise helpless
Goals for My Presentation This Morning

- To share our aspirations, processes, progress, learnings and challenges at a high level
- To address some issues and questions that have arisen
- To honor n-Lorem pioneer patients
- To enlist your support in driving needed reforms
- To take another step in bringing us all together in cohesive, effective community
n-Lorem, a Dream of Hope and Treatment for Nano-rare Patients Being Realized

Stanley T. Crooke, Md, PhD
Founder, CEO and Chairman of the board
n-Lorem’s mission is to apply the efficiency, versatility and specificity of antisense technology to charitably provide experimental antisense oligonucleotide (ASO) medicines to treat patients with nano-rare diseases (<30 patients worldwide).
n-Lorem is Committed to Equitable Distribution of ASO Treatments

- All patients are considered for potential treatment irrespective of financial means

- Directed research grants
  - Enhance our ability to invest in basic research on some genes and diseases
  - Enhance and broaden our investment in necessary infrastructure
  - We ask all directed research donors to also contribute to the general fund that benefits all patients

- Priority is given to those patients who are progressing rapidly and severely ill
  - All other patients are served as rapidly as possible in order of acceptance of the application
Nano-rare: 1 to 30 Patients Worldwide

- Nano-rare: 1 to 30 patients worldwide
- Micro-Rare: 30 to 200 patients
- Ultra-Rare: <12,000 patients
- Rare: 400K to 500K patients
- Common: millions of patients

Genetic Multi-factorial
Nano-rare: (1-30 Patients in the World)

**Isolated and Desperate**

Most nano-rare patients are never diagnosed

Average time to diagnosis is 8 years (according to UDN)

Though each patient is unique, there may be millions worldwide

**Limited to No Options**

Mutation-driven drug discovery and development

Standard commercial model cannot work for nano-rare patients

Novel nonprofit model required
Our First 173 Applications: Significant Range in Time From Symptom Onset to Diagnosis

Time to diagnosis  # of years
Average  4.32
Median  2

Time range: 1 month – 36 years
Patient #001: TGOF/LOF mutation in SCN2A
Known to exist in 9 patients worldwide

### History
- Hospitalized initially at **one month**
- First seizure at **eight months**
  - hospice care at age 2
- **29** hospitalizations at **9** institutions
- More than **34** different diagnoses
- Treated with as many as **12 to 15** drugs at a time, but **today untreated**

### Current Phenotype
- **13 years of age**
- Modest seizure activity
- Severe movement disorder
- Developmental delays
- GI issues

### Diagnostic and Treatment Odyssey
- Parents found and paid for an academic scientist to sequence patient
- Parents supported research to define the nature of the mutations and to demonstrate causality
- Many challenges in identifying an institution willing to consider an experimental treatment
- **ASO treatment planned for 2023**
ASO Technology Makes n-Lorem Feasible

- **Rapid and efficient**
- **Versatile**
  - Multiple post-binding mechanisms
  - Multiple routes of administration
  - Multiple organs
- **Validated and well understood**
  - Potent
  - Pharmacokinetics
  - Integrated safety databases

- **Cost effective**
  - Sophisticated automation: rapid, inexpensive, optimal ASO discovery
  - Potent and long-lasting ASO effects
  - Low manufacturing cost

- **Scalable**
- **Supported** by regulatory authorities
Regulatory Support Established – ASO Guidance Issued

- FDA response to n-Lorem concept supportive
- n-Lorem posed questions that require policy decisions, but progress toward policies evident
- In the meantime, experience facilitating ASOs for individuals provides real-life guidance
- Initial FDA guidance for ASO for patients with diseases caused by ultra-ultra-rare mutations: Jan. 4, 2021
- Pre-clinical requirements: Detailed guidance April 2021
- CMC guidance Dec 2021
- Clinical guidance Dec 2021
Industrialization of Experimental ASO Treatment of Nano-rare Patients

- Maximize the **quality** of every step in the process of creating, administrating, and evaluating the performance of experimental ASOs in nano-rare patients
- Established a rigorous drug discovery process enables us to be successful in identifying the most optimal ASO for development
- Assure **professional management** of clinical exposures and regulatory processes
- Maximize **learnings** from each patient and the aggregate experience
- **Scale** to meet the need

We have increased capacity for ASO discovery and development >4-fold while ensuring the highest quality at each step
## High Potency and Therapeutic Index of ASOs in the Organs

### n-Lorem Treats

### Enhance Safety and Cost Effectiveness

<table>
<thead>
<tr>
<th>Organs</th>
<th>Routes</th>
<th>Total ANNUAL dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>IT</td>
<td>500 mg</td>
</tr>
<tr>
<td>Liver</td>
<td>SQ</td>
<td>200 mg</td>
</tr>
<tr>
<td>Lung*</td>
<td>Aerosol</td>
<td>3 gm</td>
</tr>
<tr>
<td>Kidney</td>
<td>SQ</td>
<td>5-10 gm</td>
</tr>
<tr>
<td>Eye</td>
<td>Intravitreal</td>
<td>&lt;50 mg</td>
</tr>
</tbody>
</table>

* aerosol delivery to be introduced

Low dose and long duration of effect make manufacturing costs of ASO very low.
Quality Systems Established to Assure the Best Outcomes and Max Learnings....

Tertiary Care Center
Patient's genomic and phenotypic characterization

Application for Treatment to n-Lorem
Research physician + parent/patient

ATTC
Access To Treatment Committee
Assure that patient is appropriate for n-Lorem approach

n-Lorem
Drug discovery, development
Identification of optimal ASO

n-Lorem Guided
Manufacture/Sterile Fill and Finish

Food and Drug Administration
Investigator-initiated IND submission based off FDA guidance for n-of-1 ASOs

Treatment
Investigator-initiated IND begins
## Current n-Lorem Process To Discover and Develop Optimal RNase H1 ASOs for CNS Disease

<table>
<thead>
<tr>
<th>Screening Step</th>
<th>Purpose</th>
<th>Approximate Minimum Numbers of ASOs Evaluated</th>
<th>Minimum Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASO design including in silico off-target assessment</td>
<td>Exclude motifs associated with ASO structure, repeat sequences, cytotoxicity, pro-inflammatory effects and off targets</td>
<td>Scan entire pre-mRNA</td>
<td>All important attractive motifs included, unattractive excluded</td>
</tr>
<tr>
<td></td>
<td>Include attractive motifs</td>
<td>Apply algorithms</td>
<td></td>
</tr>
<tr>
<td>Primary ASO screen</td>
<td>To identify optimal sites in target RNA for ASO and H-1 binding</td>
<td>500</td>
<td>&gt;80% target reduction</td>
</tr>
<tr>
<td>Dose response evaluation of multiple ASOs</td>
<td>To select at least 20 ASOs for in vivo tolerability screening</td>
<td>50-75</td>
<td>IC50 1umol (free uptake)</td>
</tr>
<tr>
<td>In vitro off-target analysis</td>
<td>To confirm selectivity of ASO for target RNA vs. any worrisome off-target</td>
<td>As many as necessary</td>
<td>~10-fold difference in IC50s for target RNA vs. off-target</td>
</tr>
<tr>
<td>BJAB Assay</td>
<td>To exclude activators of innate immunity</td>
<td>50-75</td>
<td>Less than 2-fold increase in TNF-alpha at high ASO concentrations</td>
</tr>
<tr>
<td>Single dose tolerability screening in rodents at high dose including histopathology of CNS</td>
<td>To identify optimally tolerated lead ASOs</td>
<td>20</td>
<td>Exclude poorly tolerated candidate and include ASO with an optimal therapeutic index</td>
</tr>
<tr>
<td>Repeat dose GLP 3-month rodent toxicity</td>
<td>To identify NOAEL and cell-types at risk</td>
<td>1-3</td>
<td>An attractive therapeutic index with an acceptable NOAEL</td>
</tr>
<tr>
<td>GMP Manufacturing</td>
<td>Quality ASO drug substance</td>
<td>1</td>
<td>Pure, stable drug product</td>
</tr>
<tr>
<td>Sterile Fill and Finish</td>
<td>Quality, stable and sterile ASO drug product</td>
<td>1</td>
<td>Sterile vials for administration</td>
</tr>
</tbody>
</table>
225 Applications Submitted
~100 Patient-directed Drug Discovery Programs

Patient Baseline/ Standard of Care Data Collection

Application evaluation and feasibility

ASO Discovery and Optimization

Preclinical Development

Regulatory Stages

Clinical Study and Treatment

>10
Documentation collected
Feasibility review
ATTC review
n-Lorem decision

~60
WGS/ Obtain Cells
ASO Design/ Synthesis
ASO Discovery
ASO Tolerability Screening

>10
GLP Toxicology
GMP Manufacturing
Sterile Fill and Finish

>5
IND-drafting
IND-submission

9
5 patients on treatment
2 pending IRB approval
2 IND under review FDA meetings
To Respond To The Extraordinary Demand, We Have...

- Substantially expanded and strengthened our leadership team

  Sarah Glass  
  Chief Operating Officer

  Cedrik Ngongang  
  Medical Geneticist

  Megan Knutsen  
  Dir., Foundation Project Management

  Kim Butler  
  Sr. Director of Operations

  Dr. Joe Gleeson  
  [Consultant] Part-time CMO

  Julie Douville  
  Exec. Dir., ASO Discovery & Development

  Konstantina Skouri-Stathaki  
  Dir. ASO Design & Discovery

  Jeff Carroll  
  [Consultant] Part-time Scientific Advisor

  Laury Mignon  
  Sr. Dir. Clinical Development

  Amy Williford  
  Sr. Director Communication & Donor Relations

- Enhanced our infrastructure
- Established a new laboratory, that expands our capacity by >4-fold
- Recruited an outstanding research leader and team
Support from Leaders Across All Areas of Drug Discovery, Development and Manufacturing: More than 30 Partners Supporting Nano-rare Patients

Biotech/Pharma Companies

IONIS
Biogen
Alexion
AstraZeneca Rare Disease
Alnylam Pharmaceuticals
ultragenyx
La Jolla
Takeda

Genomic Sequencing

Children’s Mercy Kansas City
Covance
GeneEd
illumina
PacBio

Pre-clinical Toxicology CROs

Charles River
KITA Nova Institute of Toxicology
Greenfield Pathology Services, Inc.

Manufacturing

ChemGenes Corporation
Cytiva
Hongene Biotech Nucleosides & Nucleotides
IDT Integrated DNA Technologies
Nitto
Parexel

Foundations Grant Organizations

The Conrad Prebys Foundation
TARGET ALS
Solve FSHD
Wolverine Foundation
Anonymous Donor
URGenT NIH Grant
J. Wood Capital Advisors

Clinical Management

Undiagnosed Diseases Network

Sterile Fill Product

Other personalized medical centers

Other

Data Partners

Across Healthcare
Anna’s Story of Hope and Help

2004: Newborn
All appearances, a healthy baby

Dec 2020: Treatment Begins

Oct 2020
Diagnosed with ALS

Dec 2020
Feeding tube, ventilator at night and can no longer hold her head up

Dec 2020
Symptomatic

Aug 2021
Dysphagic event requiring resuscitation and rehospitalization and induced coma

Sep 2021
Anna goes home

Dec 2021
Breathing on own for 1 hour, able to walk up stairs assisted

Jan 2023
More rapid stair climbing and greater stamina
Breathes on own for >12hrs/day
Voice returns

December 2020: Treatment Begins:

Dec 2020
Treatment begins

Jul 2021
Symptoms improved including Regaining ability to walk up stairs

Oct 2021
Walking a few steps, fine motor skills returning

During 2022
Continued Gains
Stairs without support, independent breathing progressively longer

Anna’s Story of Hope and Help

SMA Type I used to be the leading genetic cause of death in children under the age of 2.

2004:
Diagnosed with ALS

2020:
Symptomatic

2021:
Breathing on own for 1 hour, able to walk up stairs assisted

2022:
More rapid stair climbing and greater stamina
Breathes on own for >12hrs/day
Voice returns

2023:
Breathes on own for >12hrs/day
Voice returns

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Anna’s Story of Hope and Help

Making the impossible possible – today!

Anna: Oct. 2020
Age 15 at diagnosis of ALS
Learnings From The First 173 Patient Applications Processed

(Data cutoff: January 2, 2023)
Substantial Number of Submitted Cases Accepted

- Accepted: 78
- Declined: 57
- Out of Scope: 6
- Out of Country: 7
- In Process: 4
- Cancelled/Mistake in Submission: 7
- In Process: 4
- Out of Scope: 6
- Out of Country: 7
- Cancelled/Mistake in Submission: 7

Age Distribution:

- 0 - 2 yrs: 38
- 3 - 6 yrs: 31
- 7 - 10 yrs: 25
- 11 - 18 yrs: 24
- 18 + yrs: 48
- N/A: 7
## Varying Genotypes of Patients (147 with sufficient info)

<table>
<thead>
<tr>
<th>Gene Category</th>
<th>Genes</th>
<th># Submissions</th>
<th># Accepted</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATPase</td>
<td>ATP1A3, ATRX, ECC6</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Cell Cycle</td>
<td>CHAMP1, SZT2, NEK1, SAMD9L</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Cytoskeletal</td>
<td>GNAO1, SPTAN1, TAOK1</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>DNA Processing</td>
<td>SMCHD1, ATM, TREX1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Endoplasmic Reticulum</td>
<td>PIGN, PIGS, PIGA, PACS2</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Glycogen</td>
<td>GBE1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Ion Channel</td>
<td>KCNB1, CACNA1A, CACNA1E, CLCN7, GRIN2B, GRIN2D, SCN8A, KCNC1, KCNT1, KCNQ2, NALCN, DNAJC5, SCN2A, SCN9A, ADSSL1, KCNH</td>
<td>26</td>
<td>16</td>
</tr>
<tr>
<td>Lysosome</td>
<td>ASAH1, CLN3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Microtubule</td>
<td>TUBB4A, KIF5A, KIF1A, TUBB3, SPECC1L, MAPK8IP3</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Mitochondria</td>
<td>MT-ND1, CHCHD10, MFN2, NUBPL</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Phospholipase</td>
<td>PLA2G6</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>RNA Processing</td>
<td>EIF2AK2, UBTF, AFF4, GARS1, hnRNPH2, EIF4A2, CHASERR</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>RNA/DNA Processing</td>
<td>SETX, PURA, LMNB1, hnRPNU</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>RNA/DNA Processing, ubiquitin</td>
<td>TARDBP</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Transcription</td>
<td>TCF4, MED13L, IKBKAP, FOXG1, NAB2/STAT6 fusion, ATN1</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Ubiquitin</td>
<td>ASXL3, RHOBTB2, ERCC8, UFM1, DNAJB2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
<td>44</td>
<td>24</td>
</tr>
</tbody>
</table>
Types of Mutations Expressed in Patients Accepted for Treatment

- Gain of function: 33
- Dominant negative: 7
- Loss of function: 10
- Gain of function/loss of function: 16
- Dominant negative/gain of function: 1

Crooke et al., manuscript submitted

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The Versatility of Antisense Technology Means More Patients Treated

ASO Strategy for Each Accepted Patient

- Allele-Selective Switch to non-Allele-Selective
- Upregulation
- Allele-Selective and Splicing
- Splicing
- RNAse H1

Crooke et. al., manuscript submitted
Phenotypes Associated with the Same Mutation Can Vary

- **8 Genes** with more than one patient with the same mutation
  - Sufficient natural history data to compare
  - Sufficient current phenotype to compare

- Genes involved in a wide range of cellular functions

Crooke et. al., manuscript submitted
# Phenotype Variation in Patients with Same Mutations in GNAO1 Gene

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Functional Consequence</th>
<th>Age at submission</th>
<th>Age at symptom onset</th>
<th>Age at Diagnosis</th>
<th>Sex</th>
<th>Duration of disease</th>
<th>Presenting Symptoms</th>
<th>Current Phenotype</th>
<th>Shared Phenotype</th>
<th>Difference/Unique Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>607 G&gt;A</td>
<td>Dominant Negative</td>
<td>2.5 yrs</td>
<td>4 weeks</td>
<td>/</td>
<td>M</td>
<td>2.5 yrs</td>
<td>Seizures, hypotonia</td>
<td>Seizures, movement disorders (chorea, dystonia), global developmental delay, hypotonia</td>
<td>Seizures, movement disorders (chorea, dystonia), global developmental delay, hypotonia</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Dominant Negative</td>
<td>2 yrs</td>
<td>3 months</td>
<td>14 months</td>
<td>F</td>
<td>1 yr 9 months</td>
<td>Seizures</td>
<td>Intractable seizures, hypotonia, movement disorders (predominantly chorea, dystonia), global developmental delay, visual impairment, cortical atrophy on brain MRI</td>
<td>Seizures, movement disorders (chorea, dystonia), global developmental delay, hypotonia - Disease onset with seizure</td>
<td>Visual Impairment</td>
</tr>
</tbody>
</table>

Crooke et al., manuscript submitted
### Phenotype Variation in Patients with Same Mutations in H3F3A

<table>
<thead>
<tr>
<th>Gene</th>
<th>Mutation</th>
<th>Functional Consequence</th>
<th>Patient age at application</th>
<th>Sex</th>
<th>Age of onset</th>
<th>Age at diagnosis</th>
<th>Time to diagnosis</th>
<th>Duration of disease/ from 1st symptom</th>
<th>Presenting symptoms</th>
<th>Current phenotype</th>
<th>Shared Phenotype</th>
<th>Difference/unique phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3F3A</td>
<td>c.137C&gt;T, p.T46I</td>
<td>gain of function</td>
<td>6 years</td>
<td>female</td>
<td>?Infancy</td>
<td>1 year</td>
<td>~ 1 year</td>
<td>~ 6 year</td>
<td>Global developmental delay, hypotonia, behavioral issues (autism spectrum disorder), movement disorder (dystonia), chronic urinary retention, joints laxity, cortical visual impairment, and plagiocephaly</td>
<td>Severe global developmental delay with regression, seizures, movement disorder (dystonia), orofacial dyskinesia, hypotonia, neurogenic bladder with chronic urinary retention, severe chronic constipation, oculomotor abnormalities (minor anisocoria), and mild enlargement of cisterna magna with hypoplasia of the corpus callosum. Craniofacial dysmorphism</td>
<td>Seizures, developmental regression, structural brain defects, and facial dysmorphism</td>
<td></td>
</tr>
<tr>
<td>H3F3A</td>
<td></td>
<td></td>
<td>4 years</td>
<td>female</td>
<td>infancy</td>
<td>/</td>
<td>/</td>
<td>~ 4 years</td>
<td>Global developmental delay, hypotonia</td>
<td>Severe global developmental delay with regression, seizures, movement disorder (dystonia, orofacial dyskinesia), hypotonia, neurogenic bladder with chronic urinary retention, severe chronic constipation, oculomotor abnormalities (minor anisocoria), and mild enlargement of cisterna magna with hypoplasia of the corpus callosum. Craniofacial dysmorphism</td>
<td>Seizures, developmental regression, structural brain defects, and facial dysmorphism</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Safety of Personalized ASOs

- To date, no ASO-related severe adverse events have been reported.
- To date, no ASO-related adverse events have been reported.

Crooke et al., manuscript submitted.
Lessons We Have Learned #1

- The journey to diagnosis is long and perilous, but challenges do not end there.
- Quality systems are working.
- Natural history and clinical trial design is effective.
- All age groups represented.
- Most gene families represented.
- Despite how advanced most n-Lorem patients are today, **meaningful evidence of benefit** is observed.
- Meaningful phenotypic variations despite sharing the same mutation.
- Phenotype drift is common.
- Professional management of experimental treatment and evaluation critical.
Creating a Community for Nano-rare Patients, Families. Sharing Knowledge and All That We Learn Broadly
Empowering Patients Through Knowledge
The Patient Empowerment Program Podcast Series

Podcast Series

Patient Empowerment Program
Creating a Community of Care
We are providing a forum where the voices of patients, advocates and experts can come together focused on the nano-rare patient.

Data as of September 2023

2500+ Unique Listeners
8000+ Downloads/Views

2023 Nano-rare Patient Colloquium

Interviews

One Year Anniversary: It Takes a Rare Community
Celebrating one year of the Patient Empowerment Program podcast! May marks a year of podcasting for us, and we’re [...] with Dr. John Maraganore

Coming Together for the Nano-rare Patient
with Andy Melostra

Bits and Bytes Help Streamline Bench to Bedside
with Andy Melostra

Intro to Medical Science

The basics put in simple terms for everyone to easily understand

Medical Science 3
How Drugs are Used

Medical Science 4
Drug Discovery Platforms

Medical Science 5
Why ASO Technology?

Medical Science 6
Antisense (How we do it at n-Lorem)
Recent Publications n-Lorem, n-Lorem Programs

- Crooke, S.T., Cole, T., Carroll, J.B., Gleeson, J.G. and Tekendo-Ngongang, C., Genotypic and phenotypic analysis of 173 patients with extremely rare pathogenic mutations who applied for experimental antisense oligonucleotide treatment, *manuscript submitted*
The St. Jude Partnership: Transformative Step Benefiting Nano-rare Patients
On Oct. 4, 2023, n-Lorem announced a collaboration with St. Jude Children’s Research Hospital to accelerate the development of optimized experimental antisense oligonucleotide (ASO) medicines for pediatric patients with extremely rare genetic neurological disorders.

St. Jude and n-Lorem will initially develop two ASO treatments together through a collaboration designed to increase the capacity of the n-Lorem pipeline and to expand St. Jude’s recently formed genomic medicine program.

As part of the collaborative effort, n-Lorem is contributing its approach to ASO design and development,
The Return on Investment (ROI) for n-Lorem is Extraordinary
The ROI provided by n-Lorem

Value Components

- Direct reduction of economic impact of nano-rare diseases
- Broad reaching advances in understanding the molecular causes of health and disease
- Driving reform in our health care systems
The ROI provided by n-Lorem

Advances in Understanding Health and Disease

- Nano-rare patients are unique “experiments of nature” in which a single major variable results in profound changes in phenotype.
- Every year billions of dollars are invested in inadequate animal models of disease.
- Nano-rare patients provide the ideal “test system” to learn about health and disease and evaluate molecular effects of disease caused targeted treatments.
- Lessons to apply to all diseases and likely change current concepts about health and disease altogether.
- The value of this knowledge is enormous.
Reforms in healthcare are driven by
- New insights into the causes of diseases
- New treatments
- Poignant personal stories of triumphs over disease

Key reforms that n-Lorem can drive
- Genomic sequencing of newborns
- Integration of other “omic” platforms
- Molecular epidemiologic studies in single variable patients
- “Omic” evaluation of the molecular events driven by an effective therapeutic

Implementation of these reforms will enhance and lengthen the lives and productivity of humans around the globe
Honoring n-Lorem Pioneer Patients & Families
Advances in Therapeutics Are Always Incremental

- Cancer
- Cardiovascular diseases
- Neurological diseases
- Metabolic diseases
- Inflammatory diseases
- Rare diseases
- And advances in the treatment of nano-rare diseases will also be incremental
SPINRAZA, a Genetic Medicine For a Genetic Disease, SMA, Advanced Incrementally

Type 1 SMA  Type 2 SMA  SMA genetic testing incorporated into newborn screening

Pre-symptomatic treatment

New medicines to treat SMA

Second generation SPINRAZA

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Pioneer patients and families open a critical door for all other patients with the same syndrome
- Provide critical information that enhances the treatment of the next patients
- Provide information that enhances the precision of the evaluation of the next patients
- Encourage other patients and families to follow their lead

The knowledge provided from studying the pioneer patient provides critical information of value to all patients in that patient community
- Confirmation that the gene and mutation are truly the cause of the syndrome
- Direction about how to treat and how to measure the effects of experimental ASOs
- Better understanding of the molecular processes causing the symptoms

Jaci, Anna, Susannah and many other pioneer patients are true HEROES

But All n-Lorem Patients are Pioneers and HEROES
- Provide broadly applicable knowledge about disease processes
- In aggregate, what we will learn will change the way we think about health and disease altogether
Susannah’s Story of Hope and Help

Making the impossible possible – today!
n-Lorem is off to a Strong Start

- Applications for treatment >220, substantially exceeding expectations
- Approvals for treatment ~110, again substantially exceeding expectations
- Quality systems established and working
- To respond to the demand n-Lorem has expanded rapidly
  - Broadened senior leadership
  - Additional laboratory scientists
  - Multiple partners
- Patient support systems including podcast series, established
- Expanding to treat >1,000 patients in the next decade
- Quality model explained so that others can follow
- Exporting the n-Lorem model underway
n-Lorem, A “Corps of Discovery” for the Mind and the Heart
Join Us As We Make The World A Better Place, One Patient, One Family at a Time