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Exicure is developing nucleic acid therapeutics based on our proprietary Spherical Nucleic Acid (SNA) technology

GROWING DEVELOPMENT PIPELINE
• AST-008 Phase1b/2 preliminary results in cancer patients expected in late 2019
• Neurology clinical candidate to be nominated in late 2019
• XCUR17 Phase1 in dermatology patients complete
• Partnership with Allergan for Hair Loss disorders
• Netherton syndrome being pursued in partnership with Dermelix

BETTER UPTAKE, GREATER STABILITY
• 3-D architecture drives better uptake and greater stability
• Demonstrated local delivery in CNS, eye, GI tract, liver, lung, and skin
• Applicable for antisense, siRNA, TLR9 modulators, and splice-switching approaches

ROBUST IP & FINANCIAL POSITION
• 85+ patents issued or allowed; 125+ pending patent applications
• $70.4MM cash as of 9/30/19
• $25.0 MM upfront payment from Allergan
Spherical Nucleic Acids: a proprietary technology platform

SNAs are dense, radial arrangements of synthetic nucleic acids on a nanoparticle

SNAs could potentially be manufactured at commercial scale

Multi-gene targeting possible with one SNA
- Bi- and tri-specific SNAs enable design of completely novel therapeutic approaches

SNAs are able to utilize these therapeutic modalities:

- Antisense
- siRNA
- TLR9 activation
- Splice-switching
SNA technology is uniquely differentiated

Unlike linear oligos, SNAs enter cells via ubiquitous scavenger receptors

- SNAs have high cell uptake without encapsulation or complexation \textit{in vitro}\textsuperscript{1}
- Extra-hepatic delivery shown for SNAs in humans (\textit{in vitro}) and mice (\textit{in vivo})\textsuperscript{2}
- Extended therapeutic half-life of SNAs \textit{in vitro} = enhanced stability inside cells\textsuperscript{3}

\textsuperscript{1}PNAS, 2013, 110, p7625; \textsuperscript{2}PNAS, 2012, 109, p11975; \textsuperscript{3}Science, 2006, 312, p1027
SNA technology enables localized delivery

Traditional oligo therapies face substantial delivery challenges...

Linear oligos delivered systematically are rapidly cleared into the liver and often chemically modified for stability

SNA technology allows nucleic acids to be delivered to local sites throughout the body, expanding the potential application of nucleic acid therapeutics

SNAs are delivered locally or topically to target tissue

Successful local delivery achieved in:
- CNS
- Eye
- Skin
- GI tract
- Lung
- Liver
SNA technology is broadly applicable

**IMMUNO-ONCOLOGY**
AST-008 in Phase 1b/2 clinical development for solid tumors

**NEUROLOGY**
NHP biodistribution study showed SNA accumulation and persistence in brain

**DERMATOLOGY**
XCUR17 improved psoriasis symptoms in Phase 1 trial

**OPHTHALMOLOGY**
Enhanced distribution and persistence in retinal layers compared to linear oligonucleotides after intravitreal injection in rabbits

**GASTROENTEROLOGY**
Demonstrated activity through oral gavage in IBD mouse models

**PULMONOLOGY**
Demonstrated target engagement and activity in mice with nebulized SNA formulation

**HEPATOLOGY**
Up to 10-fold higher functional delivery after subcutaneous administration
Development pipeline

**IMMUNO-ONCOLOGY**
AST-008 (TLR9 AGONIST)
- SOLID TUMORS

**NEUROLOGY**
- FXN: FRIEDREICH’S ATAXIA
- ATXN: SPINOCEREBELLAR ATAXIA
- CLN3: BATTEN DISEASE
- undisclosed targets: AMYOTROPHIC LATERAL SCLEROSIS, HUNTINGTON’S DISEASE

**DERMATOLOGY**
XCUR17 (ANTI-IL17RA)
- PSORIASIS
- undisclosed targets: NETHERTON SYNDROME, HAIR LOSS DISORDERS

**OPHTHALMOLOGY**
undisclosed targets: UNDISCLOSED INDICATION

**PRECLINICAL DEV**
**PHASE 1**
**PHASE 2**

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1 In combination with checkpoint inhibitors
2 Mild to moderate psoriasis
AST-008 binds to and activates TLR9 receptors to upregulate the immune system

**First synthetic nanoparticle-based DNA technology for IO application**
- Enhanced cellular uptake with decreased nuclease degradation
- Higher potency than previous TLR9 agonists

Ast-008 is an SNA designed to upregulate the immune system
- TLR9 agonists turn “cold” tumors “hot” by activating anti-tumor T-cells and natural killer cells
- In combination with checkpoint inhibitors, activating TLR9 has demonstrated improved responses in both naïve and checkpoint inhibitor refractory patients

Ast-008 is currently in Phase 1b/2 trial in combination with Pembrolizumab
- Preliminary data readout expected in late 2019
Activity was observed in AST-008 in a variety of preclinical models

AST-008 + anti-PD-1 is more active than linear oligo + anti-PD-1 in breast cancer model

AST-008’s unique architecture allows for fast, stable uptake and higher potency compared to other TLR9 agonists

- Demonstrated activity via intratumoral, subcutaneous or intravenous administration in animal models of bladder, breast, colorectal, lung, melanoma

Activity was observed in combination with PD-1, PD-L1, CTLA4 and IDO inhibitors and as monotherapy

Nucleic acid used in AST-008 was shown to be safe in over 3,000 people in a Pfizer clinical trial

- Linear oligo was safe, but was not efficacious
- Efficacy could be enhanced with SNA technology
AST-008 in Phase 1b/2 trial in combo with Pembrolizumab

Phase 1b dose-finding stage
*(preliminary results expected late 2019)*
- Open label, intratumoral administration of AST-008
- Expected enrollment of 18 patients with advanced, palpable solid tumors
  - Prioritized cancers: merkel cell carcinoma, cutaneous squamous cell carcinoma, melanoma, head & neck squamous cell carcinoma
- Enrolling checkpoint inhibitor naïve or refractory patients
- Identifying recommended Phase 2 dose, safety, PK, PD and efficacy

Total of 13 patients dosed across first four cohorts as of November 1, 2019
- No treatment related SAEs or DLTs to date

Phase 2 expansion stage
- Select pathology based on results from Phase 1b results
- Two-stage Phase 2 enrolling up to 29 patients; optional additional 10 patient cohort
- Expect to enroll PD-1 or PD-L1 antibody refractory patients
- Safety, PK, PD, and efficacy read outs

5 clinical sites open
exicure
NEUROLOGY
Neurology SNA clinical candidate expected to be nominated in late 2019

Nusinersen is a commercially available linear oligo therapeutic to treat spinal muscular atrophy (SMA)

In a proof-of-concept nonclinical study, the SNA construct of the drug performed better than nusinersen

Compared to nusinersen, the SNA construct:
- Doubled the levels of healthy full-length SMN2 mRNA and protein in SMA patient fibroblasts
- Prolonged survival by 4x (maximum survival of 115 days vs 28 days for nusinersen-treated mice)
  - Mitigated the toxicity of nusinersen in mouse model
- Showed higher persistence in CNS and lower clearance through kidney in rat biodistribution model

SNA treated survive 4X longer than nusinersen treated mice

Survival data presented at 2018 Annual Cure SMA Conference
SNAs showed higher persistence and lower clearance compared to nusinersen
NHP biodistribution data show SNA penetration to all brain regions
SNAs distribute widely throughout the brain of non-human primates

NUSINERSEN ALONE

High levels of drug present in CNS (5 SUV)

OUR SNA

Drug still present in CNS (0.2 SUV)
Significant unmet medical need in rare neurological disorders

**Neurological Genetic Disorders**
- Diseases with genetically validated targets known, but few disease modifying therapies exist
- Not readily addressable by traditional therapeutic modalities
- Significant unmet medical need in rare neurological disorders:
  - Spinocerebellar ataxia, Friedreich’s ataxia, Batten disease, Ataxia telangiectasia, Angelman syndrome, Huntington’s, ALS

We expect to nominate our first SNA neurology clinical candidate in late 2019

**EXICURE OPPORTUNITY**
Higher potency and longer persistence suggest potential advantages for frequency of dosing and therapeutic efficacy in neurological disorders
November 2019, initiated a partnership with Allergan to discover and develop two SNA-based treatments for hair loss disorders

- Exicure responsible for discovery and others costs prior to option exercise by Allergan
- Allergan responsible for all costs after option exercise

Up to $725MM in development, regulatory and sales milestones

- $25MM upfront payment
- $10MM payment to option a program or request Exicure to perform IND-enabling studies
- Additional $15MM option payment if Exicure performs IND-enabling studies
- Development and regulatory milestones of up to $97.5 million per program
- Commercial milestones of up to $265 million per program
- Tiered royalties of mid single-digit to mid-teen percentage
In February 2019, initiated a partnership with Dermelix targeting Netherton syndrome and up to 5 additional rare skin indications

- Dermelix responsible for clinical development

Up to $166M in development, regulatory and sales milestones per indication

- $1M upfront
- Additional $1M for each option exercised (up to 5)
- All development funded by Dermelix
- Low double-digit royalties on annual net sales
XCUR17: a topically applied antisense SNA dermatology clinical candidate

Phase 1 commenced April 2018 in patients with psoriasis
• 21 patients enrolled and completed dosing
• XCUR17 gel applied daily over 26 days
• 11 of 21 patients receiving the high strength XCUR17 gel showed an improvement in psoriasis symptoms (erythema, redness and induration)

Highest strength XCUR17 gel showed a statistically significant improvement in psoriasis symptoms versus the vehicle gel across the 21 patient cohort
• No XCUR17-related AEs were observed
• No relevant changes in mean psoriatic infiltrate thickness were observed for the 3 XCUR17 gels or the active ingredient-free vehicle gel

Key biomarker data from patient biopsies
• Decrease in the levels of psoriasis and inflammation markers downstream of XCUR17’s target, IL-17RA
• Statistically significant reduction in keratin 16 expression, a key marker of psoriasis (p=0.002)
• Reductions in the major inflammatory markers beta defensin 4A, interleukin 19, and interleukin 36A versus psoriatic skin at baseline

First activity was observed of nucleic acid therapy in skin disorders

Successfully administered SNAs to the skin through gels.
SNA technology also presents encouraging preclinical therapeutic benefits in ophthalmological genetic disorders:

- Distributes to both posterior (retinal) and anterior (cornea) ocular structures
- Exhibits higher distribution and persists longer compared to linear oligonucleotide
- Does not cause inflammation in the eye

Intravitreal injection of fluorescent-labeled SNA or linear oligo (in rats)

Tissue harvested 3 hours following intravitreal injection

Arrows indicate ganglion cell layer in the retinal surface
Significant unmet medical need in ophthalmological genetic disorders

**Ophthalmological Genetic Disorders**
- ~250 rare diseases with known genetic targets:
  - Leber’s congenital amaurosis 10 (LCA-10)
  - Usher syndrome type 2
  - Retinitis pigmentosa
  - Stargardt disease
  - Vitelliform macular dystrophy / Best disease
  - Choroideremia
  - Age-related macular degeneration
  - Macular edema
  - Diabetic retinopathy
  - Corneal graft rejection
- Few if any options for treatment, often leading to progressive loss of vision
- Uniquely addressable with nucleic acid therapeutics

**EXICURE OPPORTUNITY**
Currently evaluating available indications with easily identifiable patient populations and a clear path to market
SNA technology is protected until 2030 or beyond.

**BROAD IP PROTECTION**

SNAs can be used with our own newly developed oligonucleotide investigational therapeutics or can be used with other existing drugs.

**NEW & EXISTING THERAPIES**

SNAs can be administered via any non-systemic approach, including intratumoral, intra-lymph node, topical, intravitreal, etc.

**ADMINISTRATION OPTIONS**

SNAs are readily manufactured and employ digital design capabilities, making them more affordable than traditional therapeutics.

**LOW DEVELOPMENT COST**

SNAs allow for multi-gene targeting on a single SNA to address up to three genetic targets with a single drug.

**MULTI-GENE TARGETING**

SNAs are a uniquely differentiated technology approach that is applicable for antisense, siRNA, TLR9 modulators, and splice-switching approaches.

**UNIQUELY DIFFERENTIATED**

SNAs are built on strong fundamentals and are readily manufactured and employ digital design capabilities, making them more affordable than traditional therapeutics.

**PLATFORM OPPORTUNITY**

SNA platform technology has broad disease applications.

**PLATFORM OPPORTUNITY**

SNA technology allows for unprecedented local delivery of nucleic acid therapies, with better uptake and greater stability.

**SOLVES DELIVERY PROBLEMS**

SNAs allow for multi-gene targeting on a single SNA to address up to three genetic targets with a single drug.

**MULTI-GENE TARGETING**
### Extensive IP Portfolio

**METHOD OF USE**
- Administration of oligonucleotide functionalized nanoparticles to skin

**MECHANISM OF ACTION**
- Antisense inhibition by oligos bound to inorganic nanoparticles
- Immuno-modulatory SNAs

**COMPOSITION OF MATTER**
- Methods of modulating nanoparticle uptake via oligo surface density
- SNAs comprising cross-linked oligonucleotides
- siRNA modified nanoparticles

**DRUG SPECIFIC**
- AST-008; XCUR17; TNF antisense sequences and chemistries

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Exclusive, WW license to make, use and sell SNAs for therapeutic applications

IP portfolio includes 85+ issued or allowed patents and 125+ pending applications across multiple nucleic acid modalities

Multiple layers of protection exist extending platform coverage beyond 2030

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Achievements and Milestones

ACHIEVEMENTS:

✓ AST-008 PHASE 1 TRIAL IN HEALTHY VOLUNTEERS COMPLETE

✓ XCUR17 PHASE 1 TRIAL IN DERMATOLOGY PATIENTS COMPLETE

UPCOMING MILESTONES:

❑ AST-008 Phase1b/2 preliminary results cancer patients expected in late 2019

❑ Neurology clinical candidate to be nominated in late 2019

❑ Phase 2 portion of AST-008 clinical trial to initiate in 2020

❑ IND application for Netherton syndrome to be submitted in 2020 (with Dermelix)
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