

Delivering on the Promise of RNAi Therapeutics

Intradigm Corporation

August 2009

Mission

To establish leadership in the discovery, development and delivery of targeted, systemic RNA interference (RNAi) therapeutics for the treatment of serious diseases

Company Overview

- Comprehensive RNA interference (RNAi) therapeutics platform comprised of
 - Proprietary delivery technologies designed to overcome well-documented siRNA delivery challenges
 - Potent siRNA sequences
 - Innovative siRNA structural features
- Initial therapeutic focus on previously “undrugable” oncology targets
 - Broad applicability of platform extends to nearly all disease areas
- Unique, high-value intellectual property position
 - Only private RNAi company with issued patents covering siRNA delivery technology, siRNA Sequences and siRNA structure motifs

Business Strategy

- Develop comprehensive and broadly-applicable RNAi therapeutic platform
 - Highlight novel RNAi therapeutic delivery technology designed to overcome multiple delivery challenges
- Establish multiple partnerships with global pharmaceutical companies for specific RNAi therapeutics based on Intradigm's platform
 - Partnership focus can span broad variety of disease areas
- Build internal pipeline of high-value RNAi therapeutic programs

Management

Experienced team with proven pharmaceutical development track record

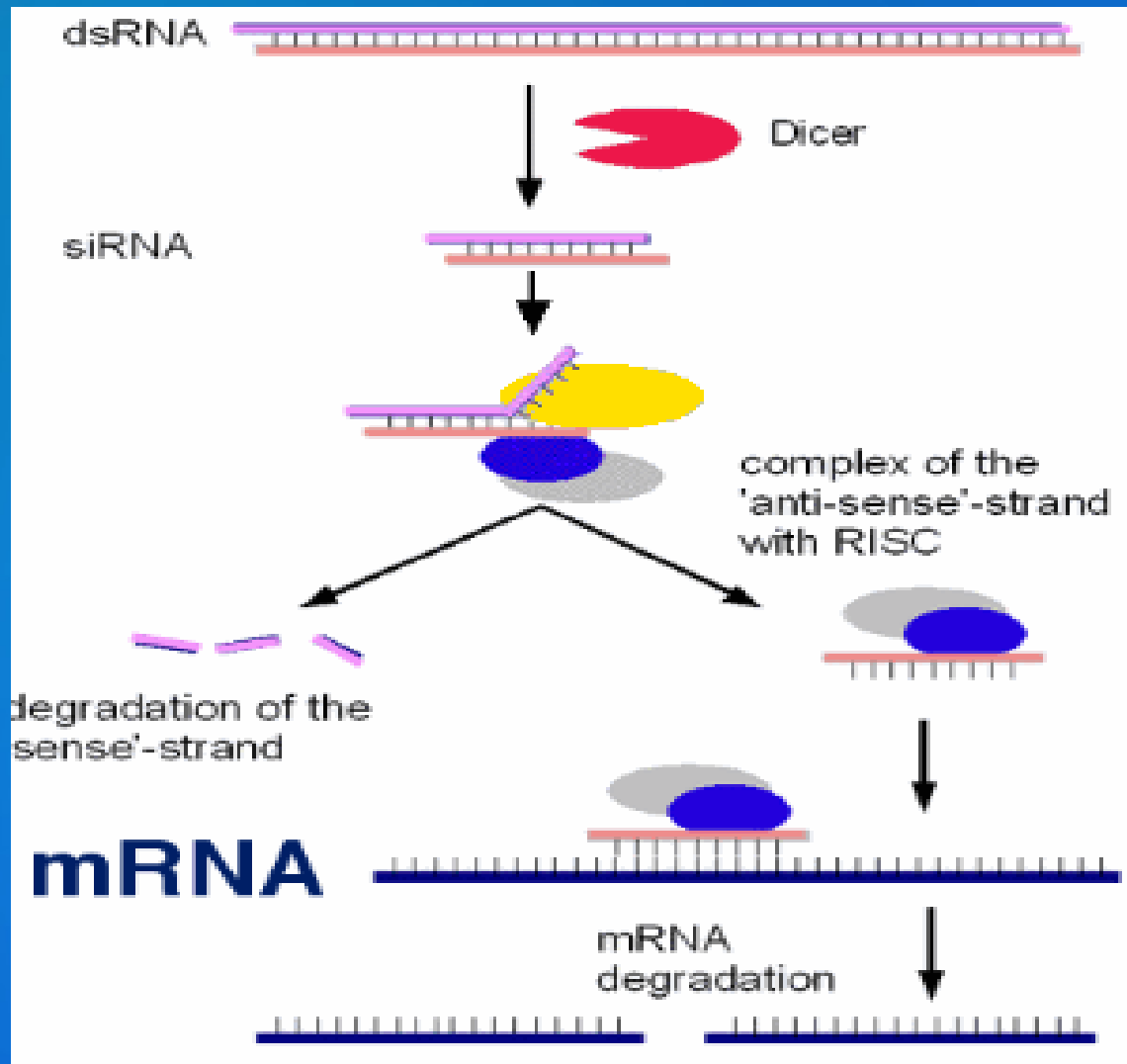
- Philip Haworth, Ph.D., CEO
 - Genencor, COR Therapeutics, Dynavax
- Xiao-Dong Yang, Ph.D., VP, Research and Preclinical Development
 - Founding scientist at Abgenix
- Samuel Zalipsky, Ph.D., VP, Technology Development
 - ALZA Corporation, SEQUUS, Enzon Inc.
- Michael Riley, M.Sc., J.D., VP, IP and Corporate Development
 - Amgen, Abgenix, Celltech Group PLC

RNAi Partnership Landscape

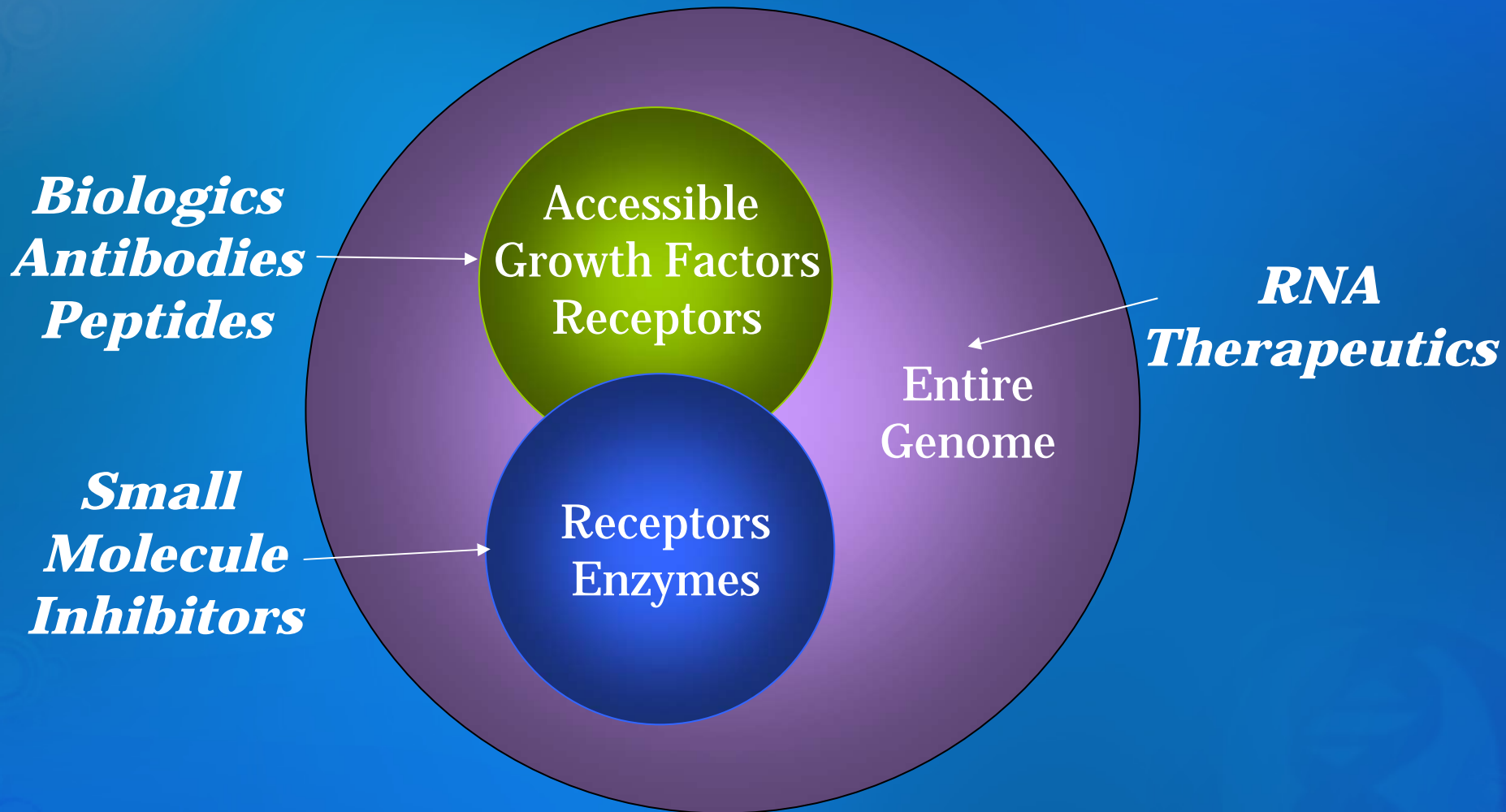
- Broad excitement for potential of RNAi
- More than 40 RNAi-related transactions with total value of more than \$5B since January 2005
 - *Merck acquires SIRNA Therapeutics for \$1.1B*
 - *Novartis/Alnylam Collaboration for \$700M*
 - *Roche/Alnylam Licensing Deal for \$1B*
 - *AstraZeneca/Silence Therapeutics Collaboration for \$400M - \$1B*
- Nearly all deals involved preclinical stage assets/programs with few involving safe and effective systemic delivery technology

Significant precedent for Intradigm's potential for entering multi-million dollar deal with drug developer(s)

RNAi Overview



RNAi Opportunities



Intellectual Property

- Impressive IP portfolio covering proprietary delivery technology, key siRNA structural features and potent siRNA sequences against more than 50 high value disease targets
 - Portfolio of over 35 issued patents and 120 pending patent applications.
- Key assets include:
 - Multiple layers of protection for PolyTran™ delivery technology
 - Exclusive license to three Zamore patent families from UMass related to broad structural features of siRNA design
 - Recent notice of allowance on 25mer double blunt ended siRNA sequence validates Intradigm sequence IP strategy

Comprehensive Approach to RNAi

RNAi Therapeutics Platform

siRNA Sequence
Identification and IP

Next-Gen Structural
Features and IP

siRNA Delivery
Platform and IP

**Intradigm Possesses Capabilities
and IP In All Three Categories**

siRNA Sequence Selection

- Intradigm possesses library of proprietary siRNA sequences against more than 50 targets
 - 25-mer double blunted-ended siRNA molecules
 - Issued US patent
 - Identified using a combination of bioinformatics algorithms and proprietary know-how
 - Selected primarily based on extremely high potency (IC₅₀= 10 – 200pM)
 - Cross species sequence homology (mouse/monkey/man)

Structural Features

- Intradigm is actively exploring potentially valuable structural modifications for its siRNAs
 - Modifications intended to improve efficacy and safety, also increase depth patent protection
- Key patent portfolio licensed exclusively from UMass Medical School
 - Licensed IP includes the “Zamore Design Rules” that significantly improve the potency and efficacy of RNAi therapeutics

RNAi Delivery Challenge

The challenge of delivering siRNAs:

- Create a safe and effective systemic delivery technology that enables the delivery of RNAi therapeutics to specific tissues
- Enable intracellular delivery and cellular uptake
- Overcome inherent biological instability of siRNA molecules
- Address potential toxicities such as immunogenicity and cytokine release caused by siRNAs and/or delivery vectors

Intradigm is developing novel delivery technology that overcomes these issues

Intradigm's Delivery Solution

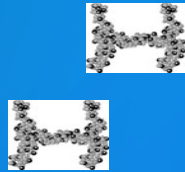
- Intradigm has developed a proprietary process for creating nanoparticles that combine active siRNA molecules with biodegradable polypeptides
- Safe, systemic delivery of siRNA sequences
 - Capable of intracellular delivery under pharmaceutically relevant conditions
 - Can incorporate any siRNA sequence against any disease target allowing for simple and rapid development of new RNAi therapeutics

Based on PolyTranTM - a proprietary family of biodegradable peptide-based polymers that are optimized for efficient siRNA delivery

RNAi Nanoparticle Formation

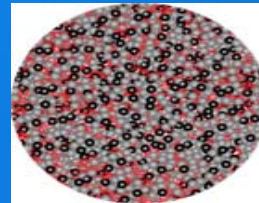
Positively charged PolyTran polymers complex with negatively charged siRNAs to form nanoparticles

**Cationic
Polymer
(PolyTran)**



siRNA

Mix siRNA and cationic polymer to form particles

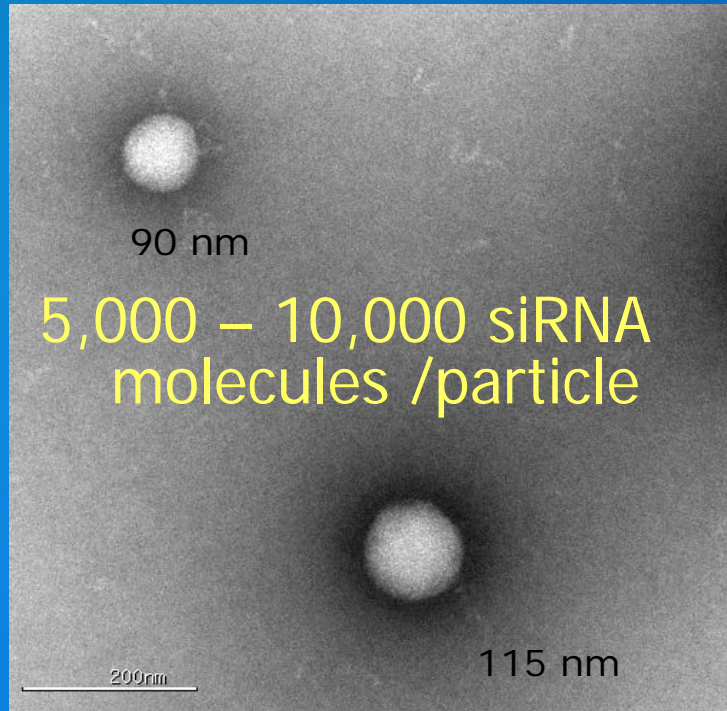


PT-Nanoparticles

RNAi Nanoparticles
~100 nm diameter

PT-Nanoparticle Characterization

Particle size
 $100\text{nm} \pm 20\text{nm}$



Activity in mouse
xenograft model

Zeta potential
 $\sim +30\text{mV}$

Pharmacokinetics
 $T_{1/2} > 1 \text{ min}$

Particle stability
 $> 21 \text{ days}$

In vivo gene knockdown

Enhanced Delivery Features

- Intradigm's nanoparticles allow a number of “modifications” designed to improve delivery:
 - PEGylation – Increase half-life, reduces immunogenicity
 - Targeting Moieties – Attachment of specific ligands enables delivery directly to targeted cells

Characterization of Prototype PEGPT-Nanoparticle

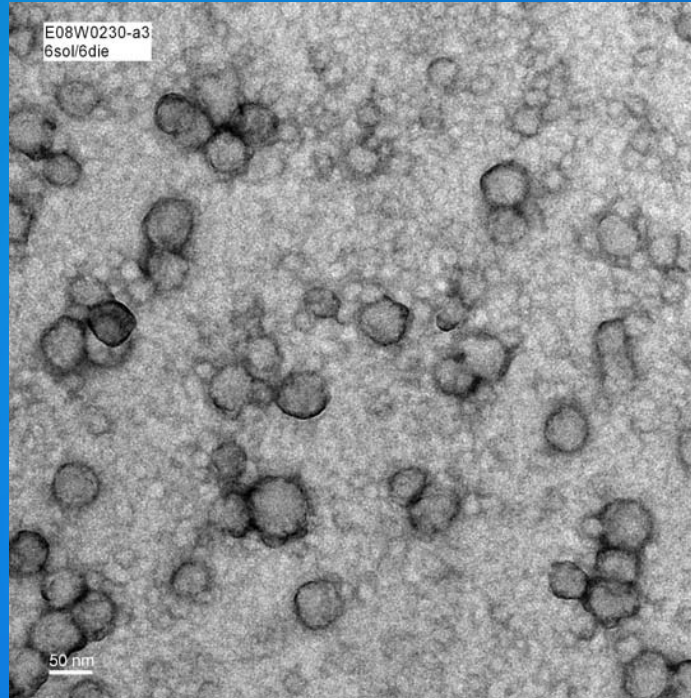
Stable to Aerosolization

Particle size
 $80\text{nm} \pm 20\text{nm}$

Tumor accum. in
mouse xenograft
model

Zeta potential
 $+10\text{mV}$

Pharmacokinetics
 $T_{1/2} > 5 \text{ min}$



Particle stability > 100 days

In vitro gene knockdown

Investor and Financing History

- Closed final tranche of \$21.4M Series B round in January 2009
 - Have raised more than \$37M to date
 - Well financed with capital to carry through 2010
- Sophisticated and strategic investor base including multiple large pharmaceutical companies
 - Alta Partners
 - Astellas Venture Management
 - Frazier Healthcare Ventures
 - Lilly Ventures
 - MediBic Alliance Investment Fund
 - MP Healthcare Venture Management
 - Novartis Venture Fund
 - Roche Venture Fund

Summary

- Comprehensive RNAi therapeutics platform
 - Delivery, sequences and structural features
- Platform has achieved preclinical proof-of-concept
- Dual-pronged business strategy focused on strategic partnerships and internal pipeline development
 - Initial internal pipeline focus on previously “undruggable” oncology targets including both solid and liquid tumors
 - Partnerships able to address nearly all disease areas
- Unique, high-value intellectual property position
- Experienced management team with proven pharmaceutical development track record

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