



**C.E. Unterberg, Towbin**  
*3<sup>rd</sup> Annual Emerging Growth  
Opportunities Conference*  
**New York City, NY**

## **Rosetta Genomics: Leading the MicroRNA Revolution**

10 July 2007

## Safe Harbor Statement

**Except for historical information, the statements made in this presentation, including those related to: the future potential of microRNA and therapeutic markets; the timing or successful completion of the Company's product commercialization activities; the projected timing of revenues; and any financial projections, including our estimated cash burn for 2007, are forward-looking statements. Such forward-looking statements involve significant risks and uncertainties that may cause actual results and events to differ materially and adversely from those implied by the forward-looking statements. Risks and uncertainties include: the fact that Rosetta's products are in the early stages of development; that no diagnostic or therapeutic microRNA products are currently approved for sale, and we cannot assure you that we or anyone else will ever develop and commercialize such a product; and that the timing of the development of diagnostic and therapeutic products, particularly conducting any required clinical trials and obtaining regulatory approval, is highly uncertain; as well as the risks and uncertainties set forth under "Risk Factors" in Rosetta's most Annual Report on Form 20-F filed with the Securities and Exchange Commission. Rosetta is presenting this information as of the date of the presentation and expressly disclaims any duty to update the information contained in this presentation.**



## MicroRNAs: A New Dimension of Biology

**“Smart scientists that we are, we managed to miss this entire class of incredibly important regulatory molecules until the 21<sup>st</sup> century.”** Eric Lander, Director, Broad Institute Science, June 2007

**“What physics was to the 20th century, biology will be to the 21st—and RNA will be a vital part of it”** The Economist, June 2007



## The Next Generation RNAi Company

- ◆ RNA Interference (RNAi) is key to protein expression
- ◆ MicroRNAs are the naturally occurring (endogenous) mediators of the RNAi mechanism
  - A MicroRNA agonist increases endogenous action (protein down regulation)
  - A MicroRNA inhibitor decreases endogenous action (protein up regulation)
- ◆ MicroRNA expression profiles correlate to disease states
- ◆ Bottom Line: MicroRNAs = Biomarker = Therapeutic Target
- ◆ Rosetta Genomics has a leading IP and technology position in microRNAs for research, diagnostic and therapeutic uses



## Building a Leading Position in MicroRNAs

- ◆ Developed proprietary bioinformatics to predict over 100K microRNAs
- ◆ Filed broad patents on microRNA genes, microRNA precursors, microRNAs and microRNA target binding sites – establishes a leading IP portfolio
- ◆ Developed in vitro system to detect and validate microRNAs against predicted sequences
- ◆ Identified hundreds of novel microRNAs (published in Nature Genetics)
- ◆ Developed extraction methodologies: FFPE, Serum, Saliva, Amniotic Fluid, Urine
- ◆ First-ever microRNA gene patent issued
- ◆ 50+ person company dedicated solely to research, development and commercialization of microRNA-based products



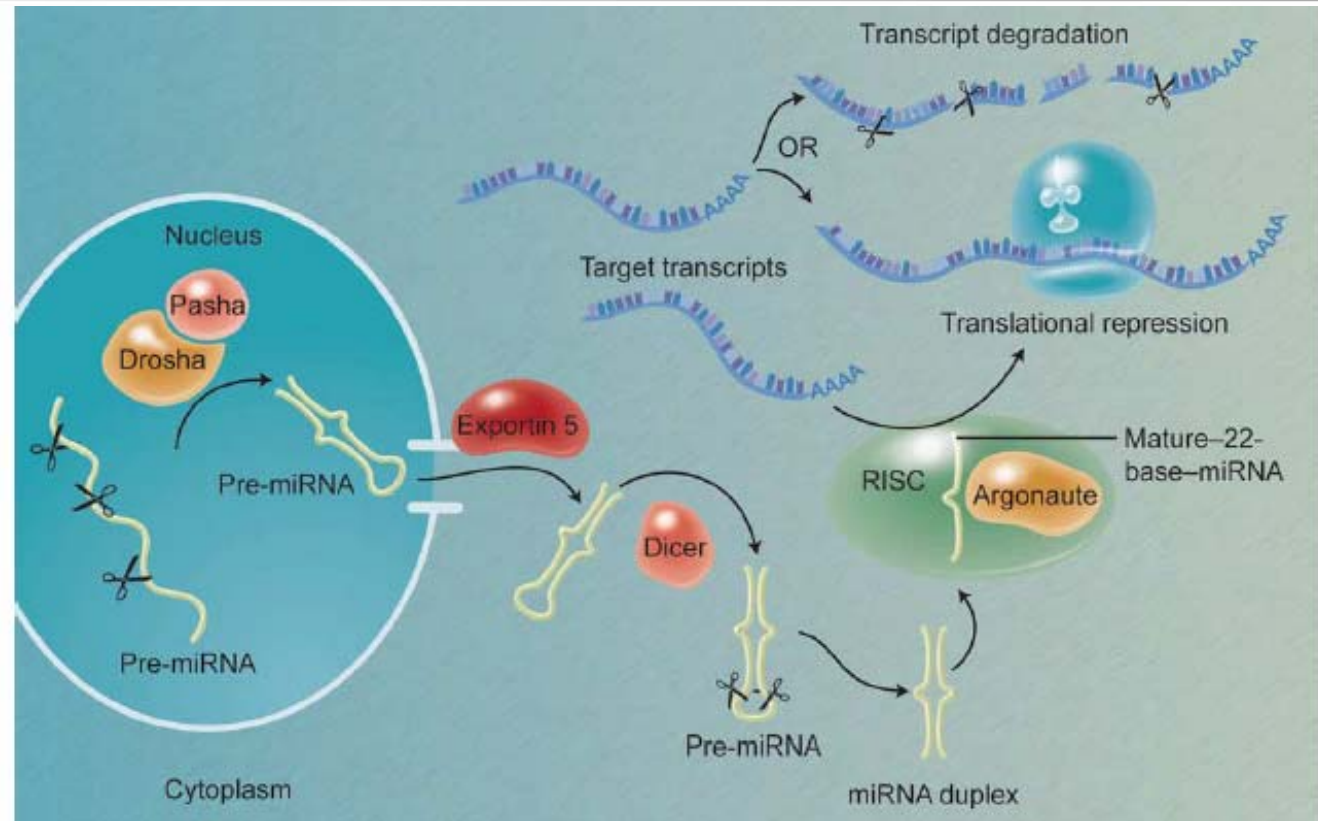
## Significant Activity in RNAi Field

- ◆ Nobel prize on RNAi, October 2006
- ◆ Unprecedented licensing, finance and M&A activity of RNA technology companies
  - Merck Acquisition of Sirna (\$1.1 BB)
  - Roche-Alnylam Collaboration (\$1 BB)
- ◆ MicroRNA a key topic in major conferences (ASH, ASCO, AACR, Keystone, CHI, Gordon)
- ◆ Extensive academic research focusing on microRNAs
  - In June, 4 papers on microRNA role as regulators of p53-mediated tumor suppression
    - Molecular Cell – Rosetta Genomics/Weizmann Institute

**MicroRNA Publications**  
Nearly doubled in 2006!

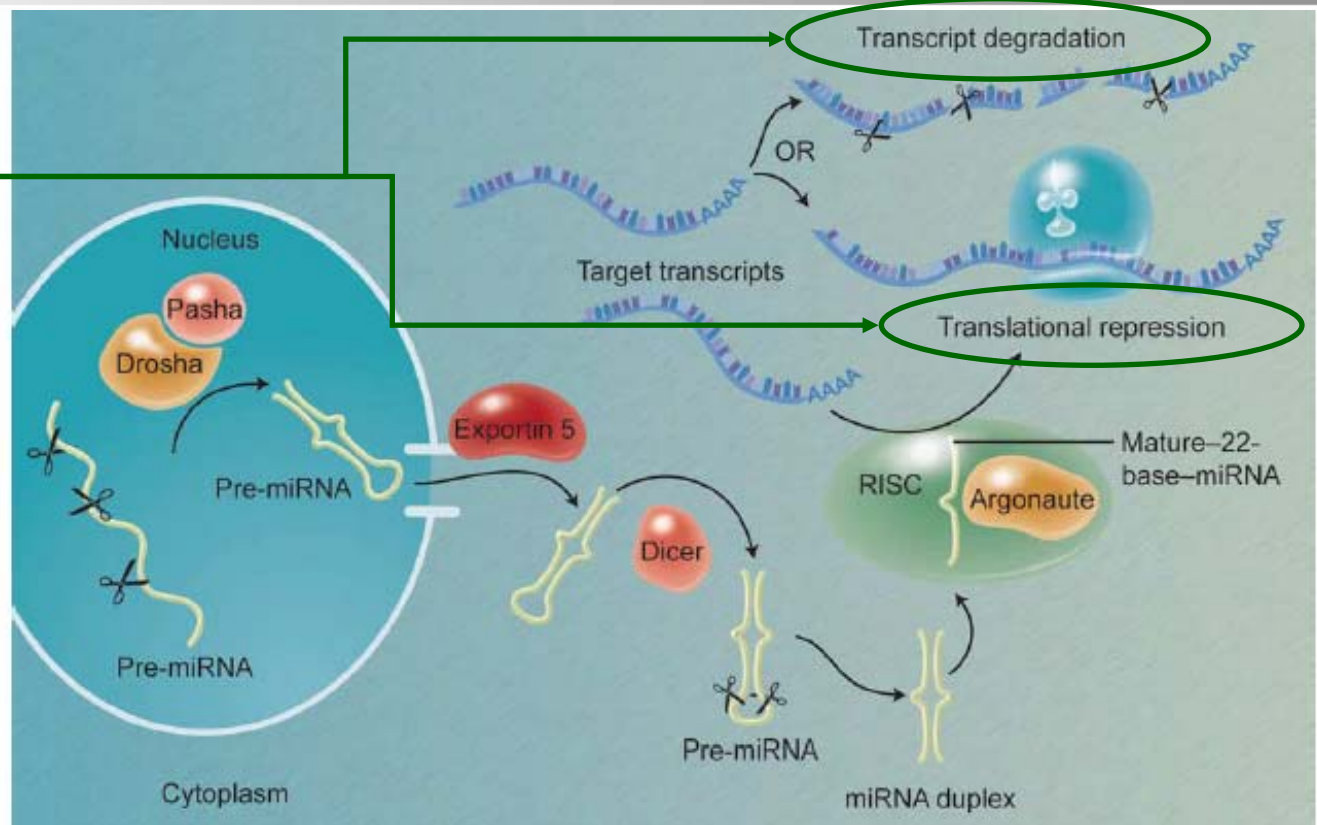


# microRNA Biogenesis

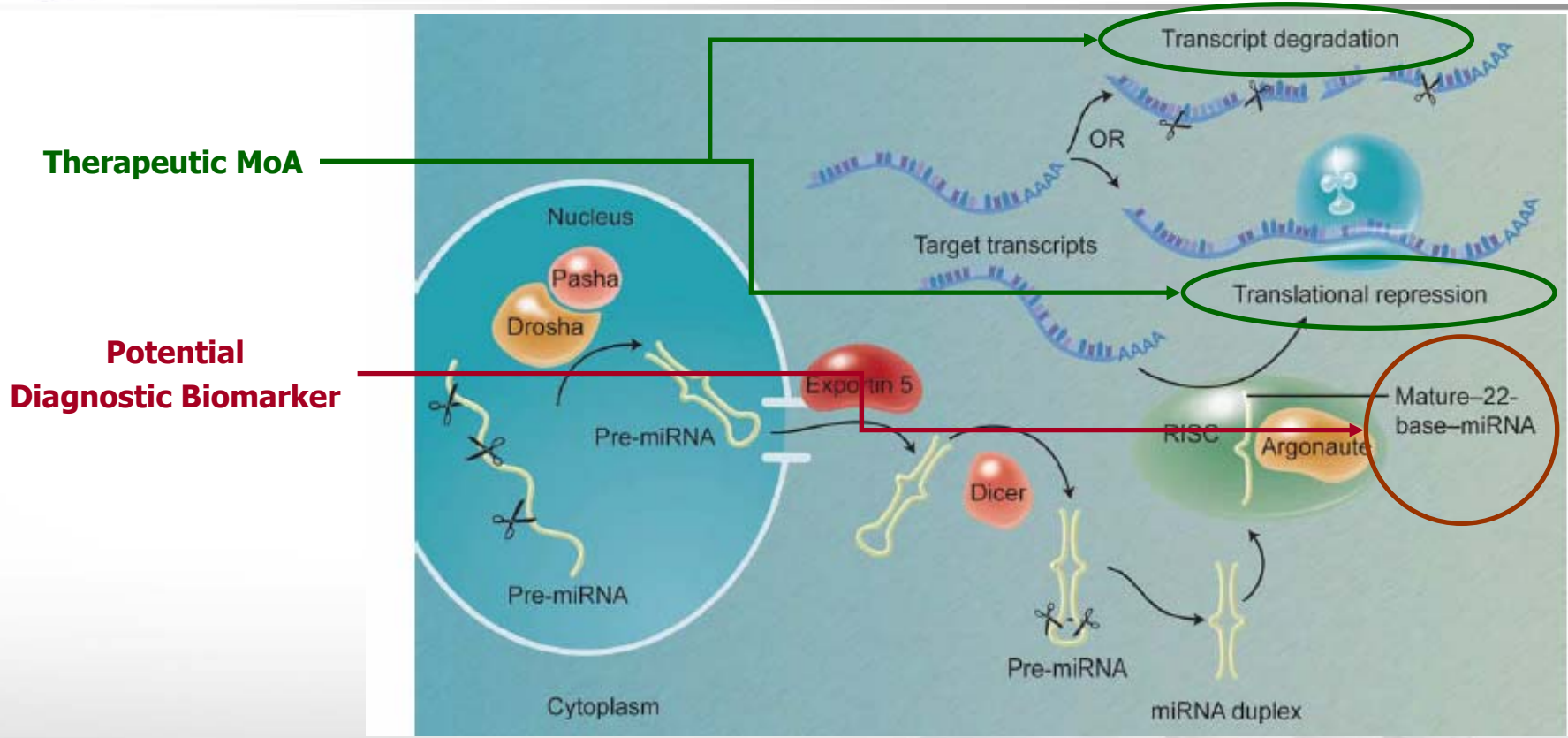


# microRNA Biogenesis

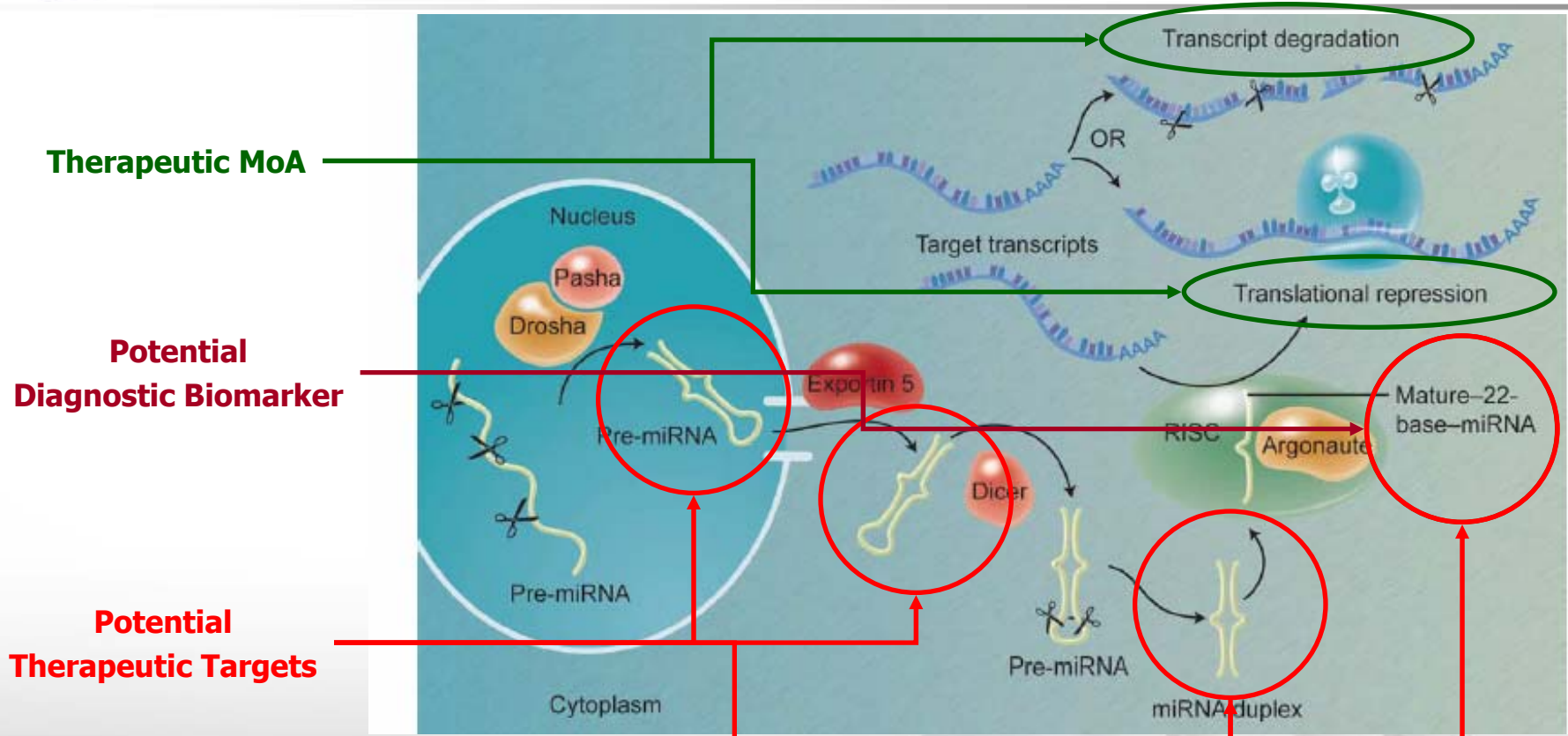
Therapeutic MoA



# microRNA Biogenesis



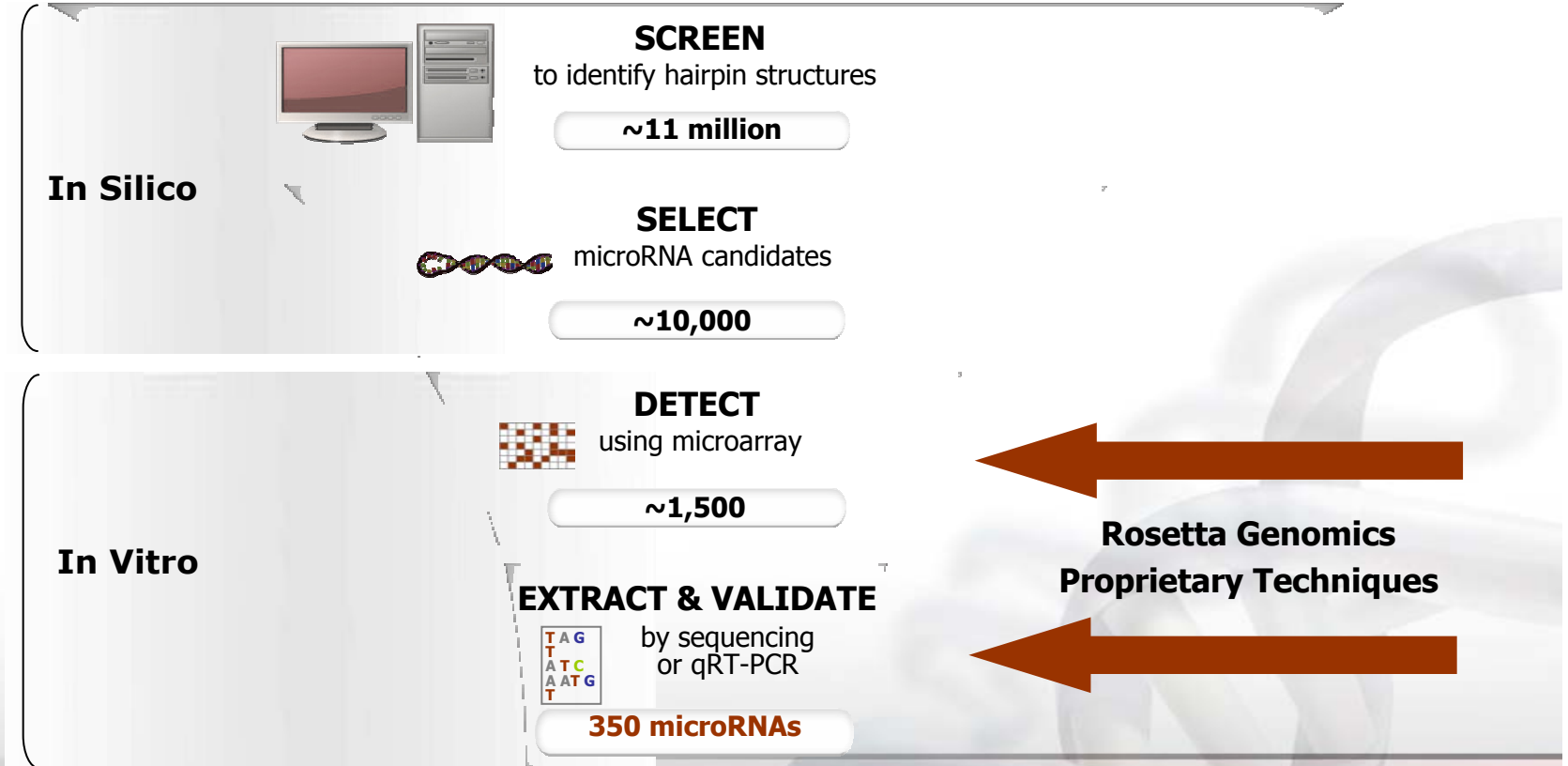
# microRNA Biogenesis



R.A. Shivdasani  
Blood Aug. 1, 2006



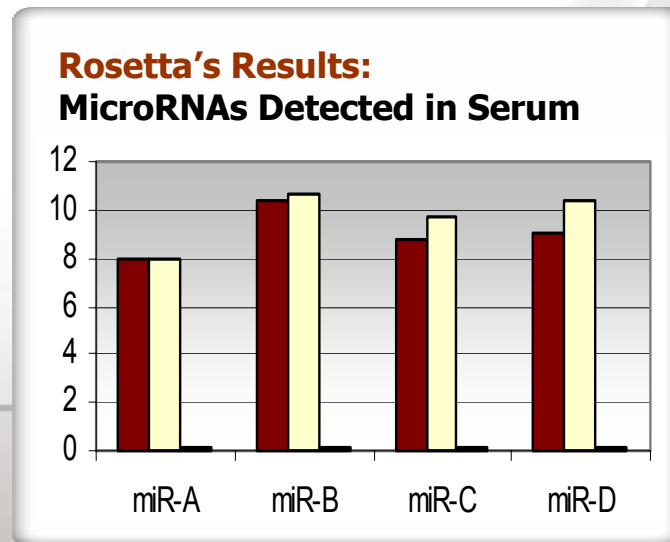
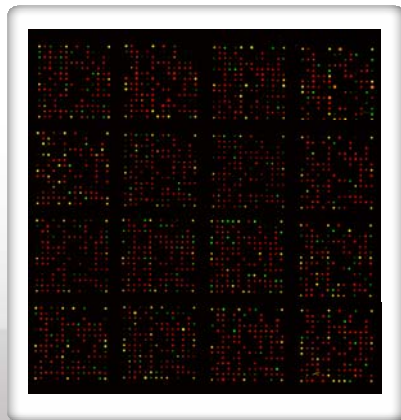
# Rosetta's Target Discovery Platform



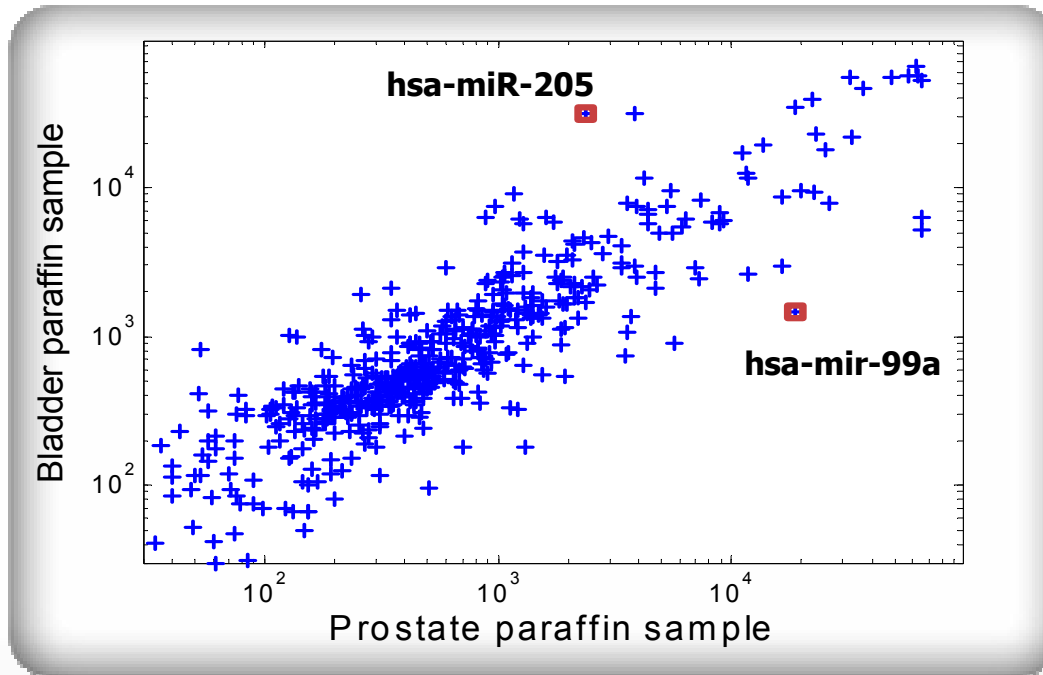
**Rosetta Genomics  
Proprietary Techniques**

## Cutting-Edge Technology Platform

- ◆ Developed proprietary technologies (miRdicator™) to detect and quantify microRNAs:
  - microRNA detection and quantification in body fluids
  - microRNAs detection and quantification in fresh and FFPE tissues
  - Assay systems with high sensitivity/specificity and low background noise

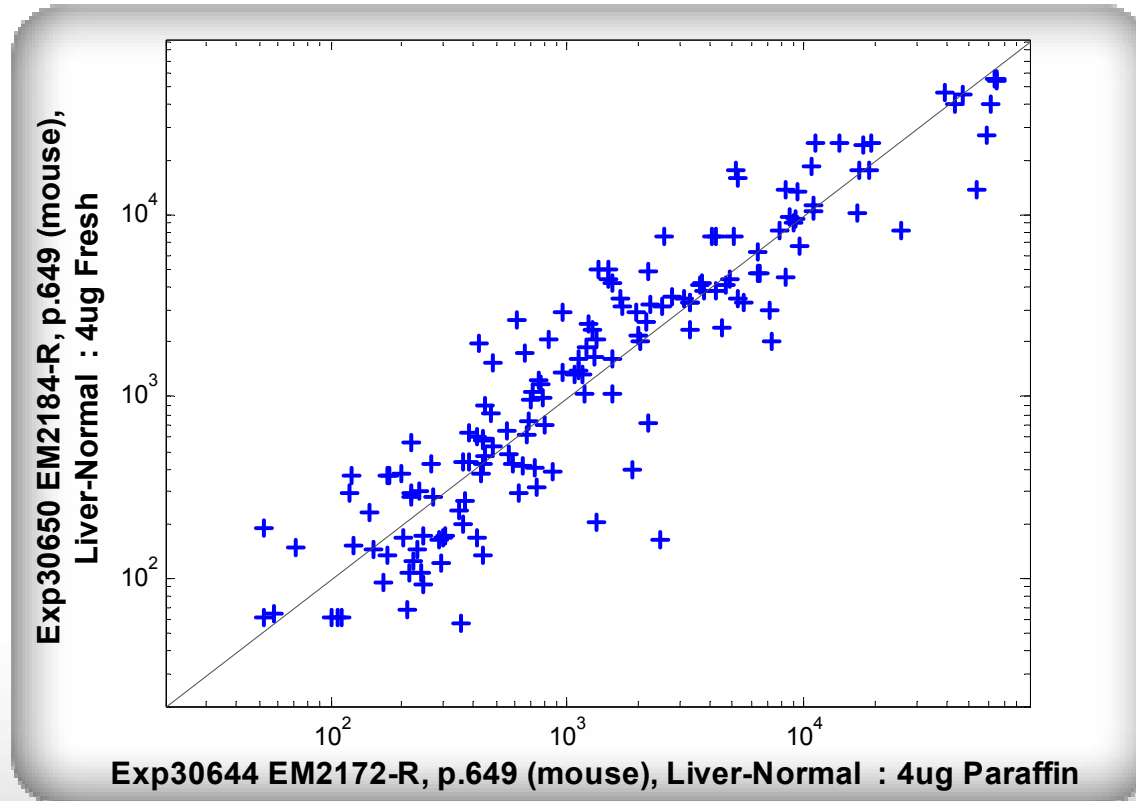


## miRdicator™ Microarray Performance: Tissue Specificity



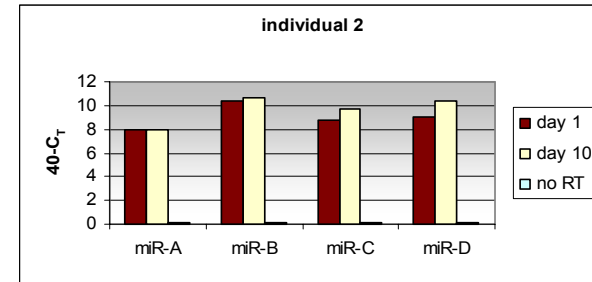
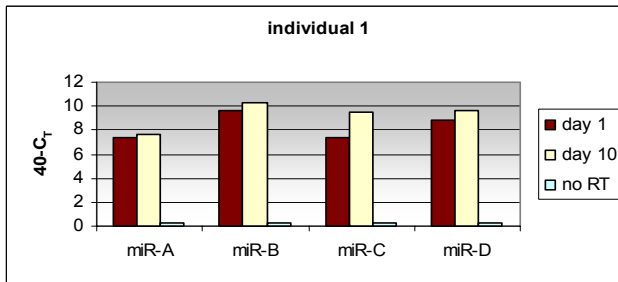
**MicroRNA expression profiles obtained from paraffin embedded prostate and bladder tissues show distinct tissue specific microRNAs**

# MicroRNA are Highly Stable in FFPE

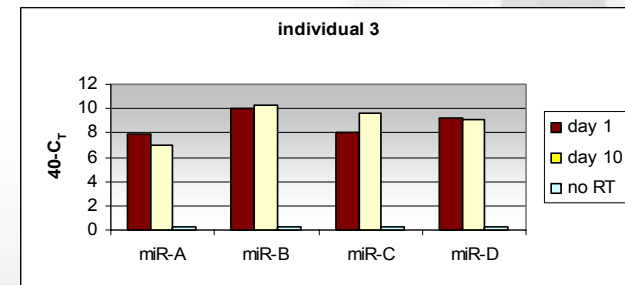


**MicroRNA expression profiles obtained from paraffin embedded liver correlate to fresh liver samples**

# MicroRNA are Highly Stable in Serum

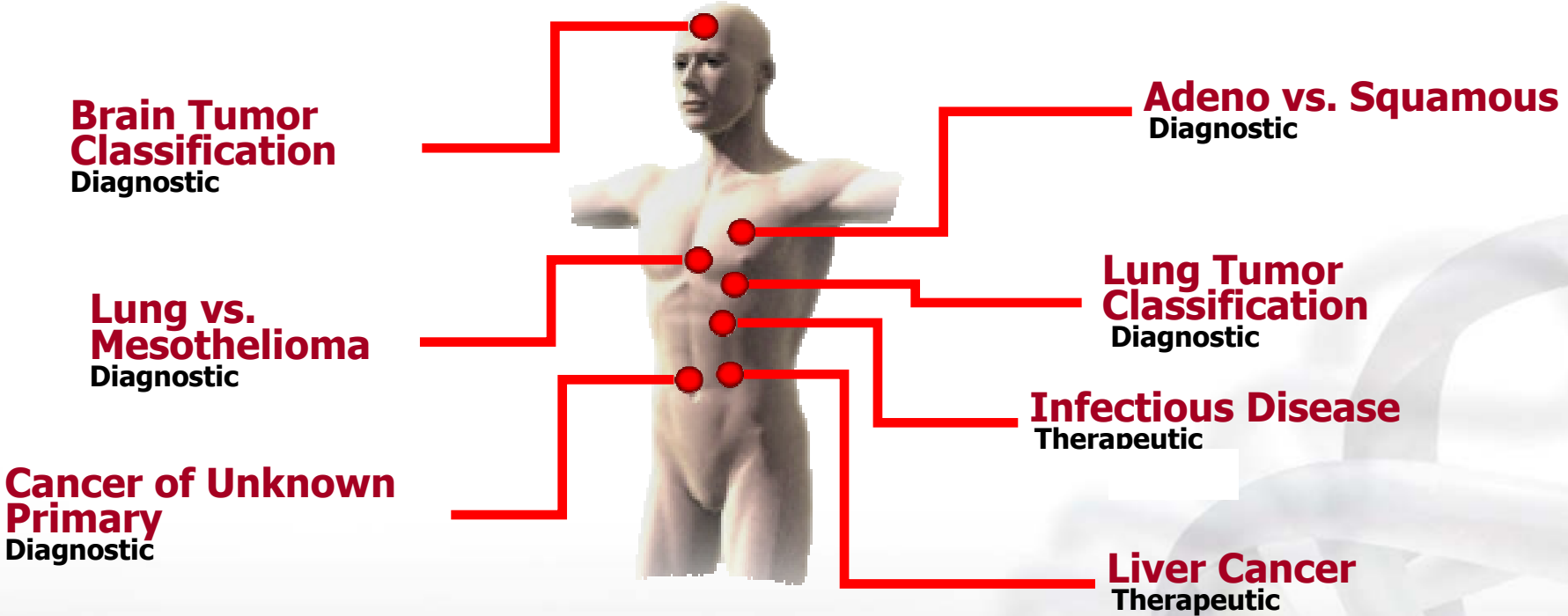


- Serum samples were taken from the same healthy individuals on different days
- qRT-PCR was performed on four different microRNAs levels





# Rosetta's Product Pipeline





## **Dx Pipeline Foundation: Cancer of Unknown Primary**

- ◆ Cancer of Unknown Primary\* (CUP) – The presence of a metastatic cancer without a known primary site of origin
  - 3-5% of all malignancies in the U.S.
  - Median survival of 3 to 4 months
- ◆ Current diagnostics inadequate
  - Must know tumor's origin to effectively treat metastases
  - CUP market opportunity ~\$200 MM annually

**\*Also referred to as Cancer of Occult Primary**



## CUP Diagnostic

- ◆ Distinguish Point of Origin in 15 tissues with 28 microRNAs\*:
  - Breast
  - Bladder
  - Cervix
  - Colon
  - Liver
  - Lung
  - Melanocytes
  - Ovary
  - Pancreas
  - Prostate
  - Small intestine
  - Stromal
  - Testes
  - Thyroid
  - Uterus
- ◆ ~800 samples screened
- ◆ Overall Accuracy ~90%
- ◆ Expected Launch – 2H2008

**\*Specifics may change in final assay development**



# On-going Dx Research Efforts

## Therapeutic Area

- ◆ Acute Myeloid Leukemia
- ◆ Brain Cancer
- ◆ Breast Cancer
- ◆ Bladder Cancer
- ◆ Colon Cancer
- ◆ Endometrial Cancer
- ◆ Kidney Cancer
- ◆ Lung Cancer
- ◆ Lymphoma
- ◆ Melanoma
- ◆ Ovarian Cancer
- ◆ Preeclampsia
- ◆ Preterm labor
- ◆ Stomach Cancer

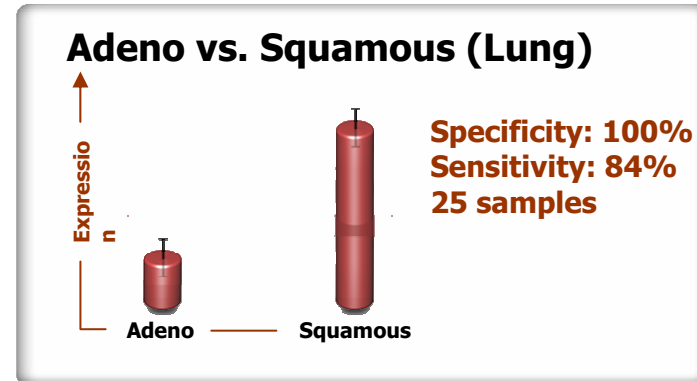
## Indication

- ◆ Early detection
- ◆ Early detection of relapse
- ◆ Early detection of recurrence
- ◆ Need for adjuvant therapy
- ◆ Prognosis
- ◆ Prognosis for patients with invasive cancer
- ◆ Response to treatment
- ◆ Risk of developing brain metastasis
- ◆ Risk of recurrence
- ◆ Risk of invasiveness
- ◆ Risk of local advance recurrence

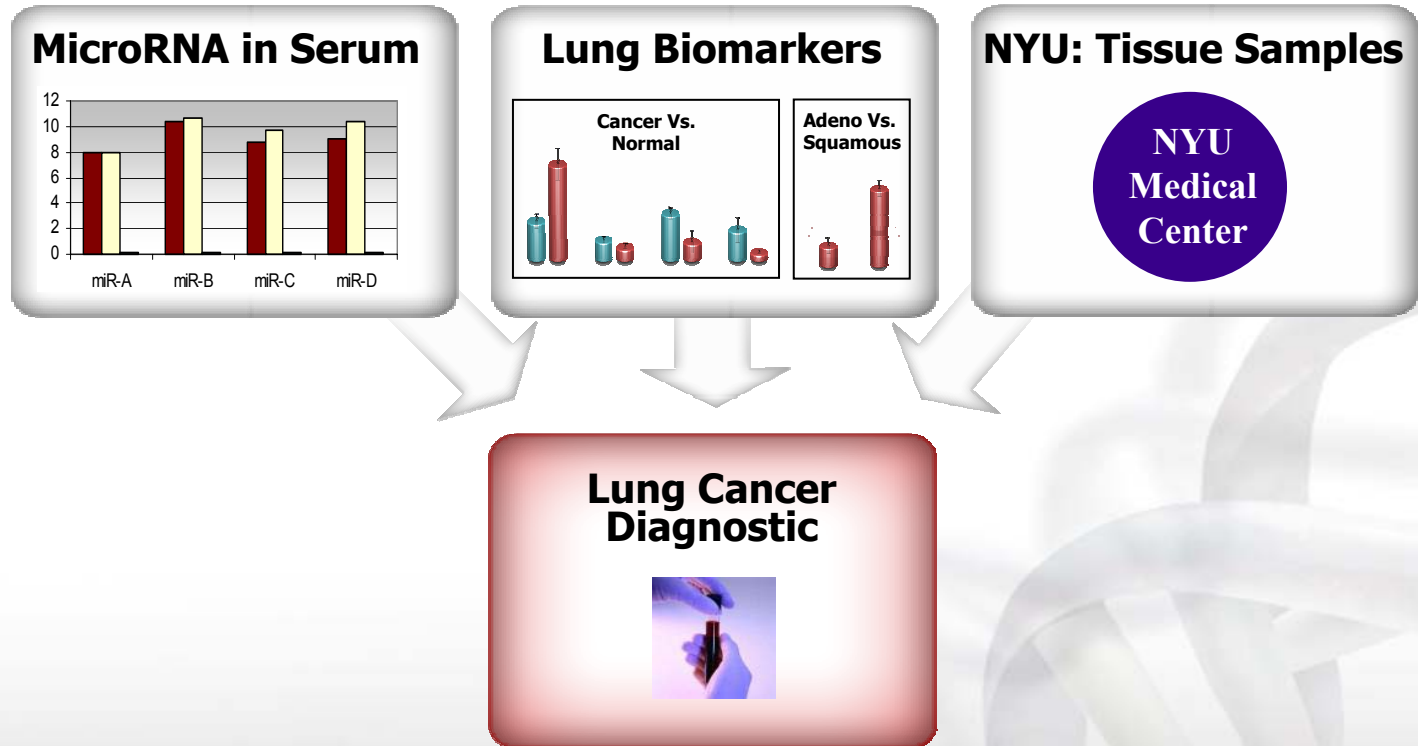
**Over 25 Diagnostic Products in Development**

## NSCLC Treatment (Adeno vs Squamous)

- ◆ NSCLC with any squamous differentiation are not candidates for Avastin® therapy
- ◆ Tumors that are clearly squamous are easy to diagnose
- ◆ Issues in pathological differentiation:
  - If the tumor sample shows adenocarcinoma, could there be an unsampled squamous component?
  - When the tumor is poorly differentiated, is there a squamous component that is hard to recognize, or is it truly a poorly differentiated pure adenocarcinoma?

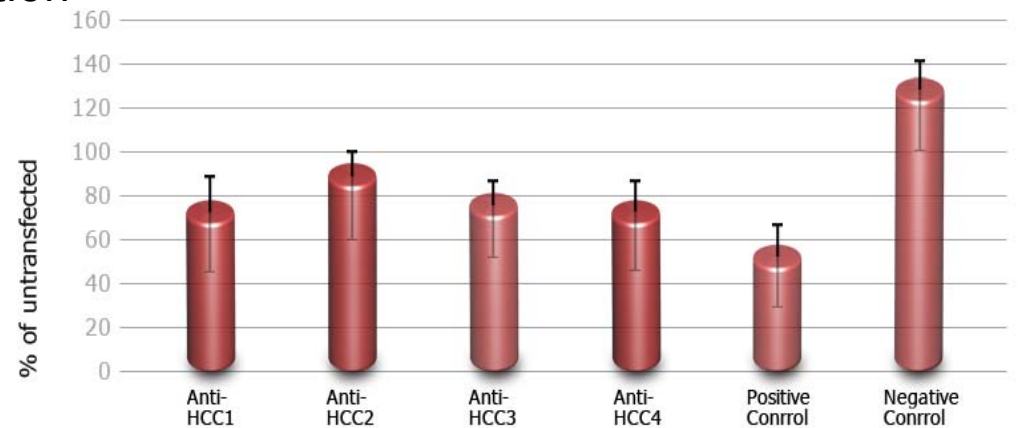


# Developing a Novel Cancer Diagnostic



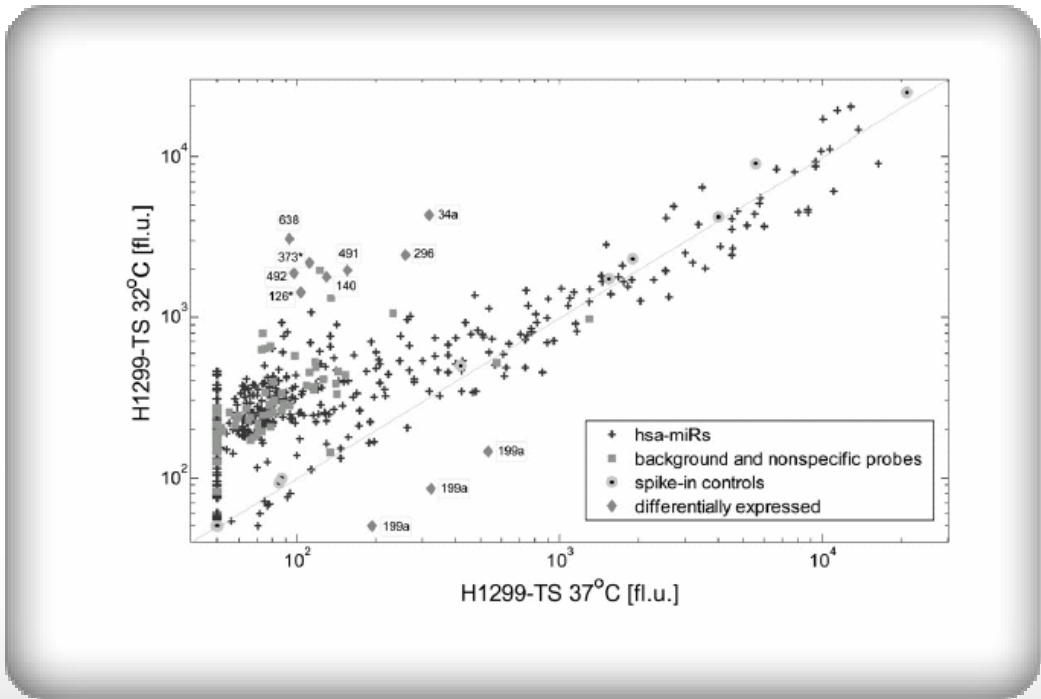
## Liver Cancer Therapeutic

- ◆ Liver cancer (HCC) is the fifth most common cancer in the world
  - <10% 5-year survival
- ◆ MicroRNA-based drug in collaboration with Isis in lead selection phase\*
- ◆ MicroRNAs are expressed differently in HCC than in normal liver
- ◆ Cell based functional assays:
  - Proliferation/growth inhibition
  - Apoptosis assay
  - Cell cycle arrest assay





# miR-34a Up-regulated by p53 – Detected by miRdicator™ Microarray



## Transcriptional Activation of miR-34a Contributes to p53-Mediated Apoptosis

Nina Raver-Shapira,<sup>1</sup> Efi Marciano,<sup>1</sup> Eti Meiri,<sup>2</sup> Yael Spector,<sup>2</sup> Nitzan Rosenfeld,<sup>2</sup> Neta Moskovits,<sup>1</sup> Zvi Bentwich,<sup>2</sup> and Moshe Oren<sup>1\*</sup>  
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\*Correspondence: moshe.oren@weizmann.ac.il  
DOI 10.1016/j.molcel.2007.05.017

Molecular Cell 26, 1-13, June 8 2007

# Intellectual Property Estate

Filed



## SCREEN

to identify hairpin structures

~11 million



## SELECT

microRNA candidates

~10,000



## DETECT

using microarray

~1,500

## VALIDATE

by sequencing  
or qRT-PCR

Academia



## VALIDATE

by sequencing  
or qRT-PCR

Rosetta Genomics



## VALIDATE

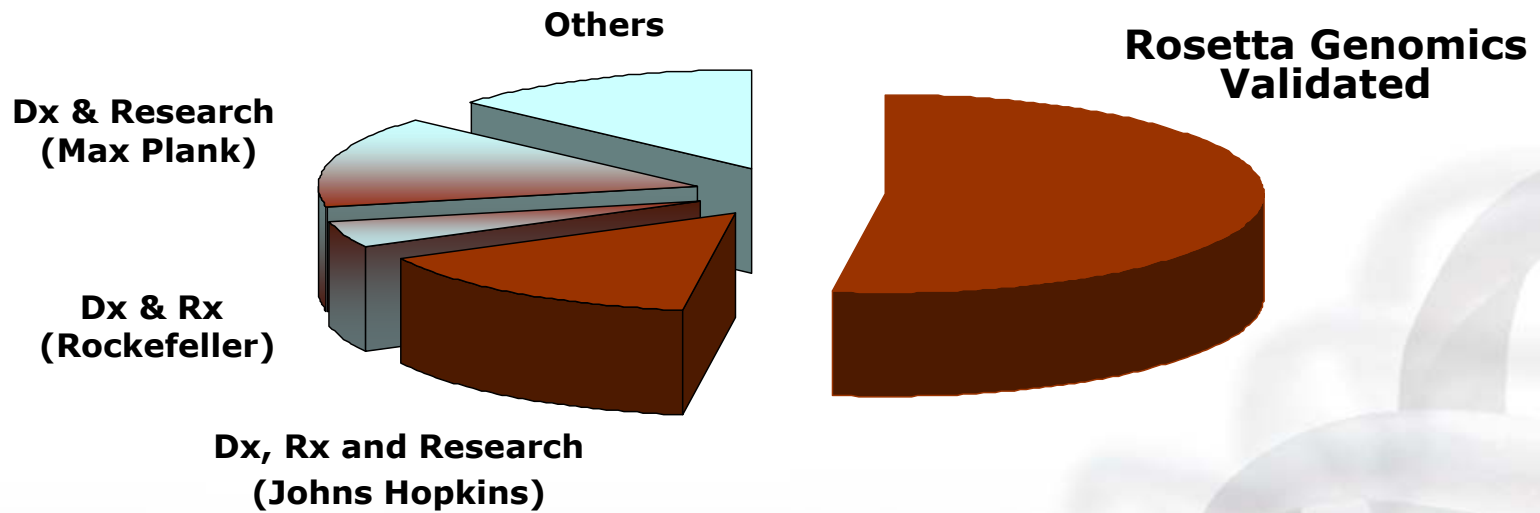
by sequencing  
or qRT-PCR

Industry





# microRNA Intellectual Property Landscape





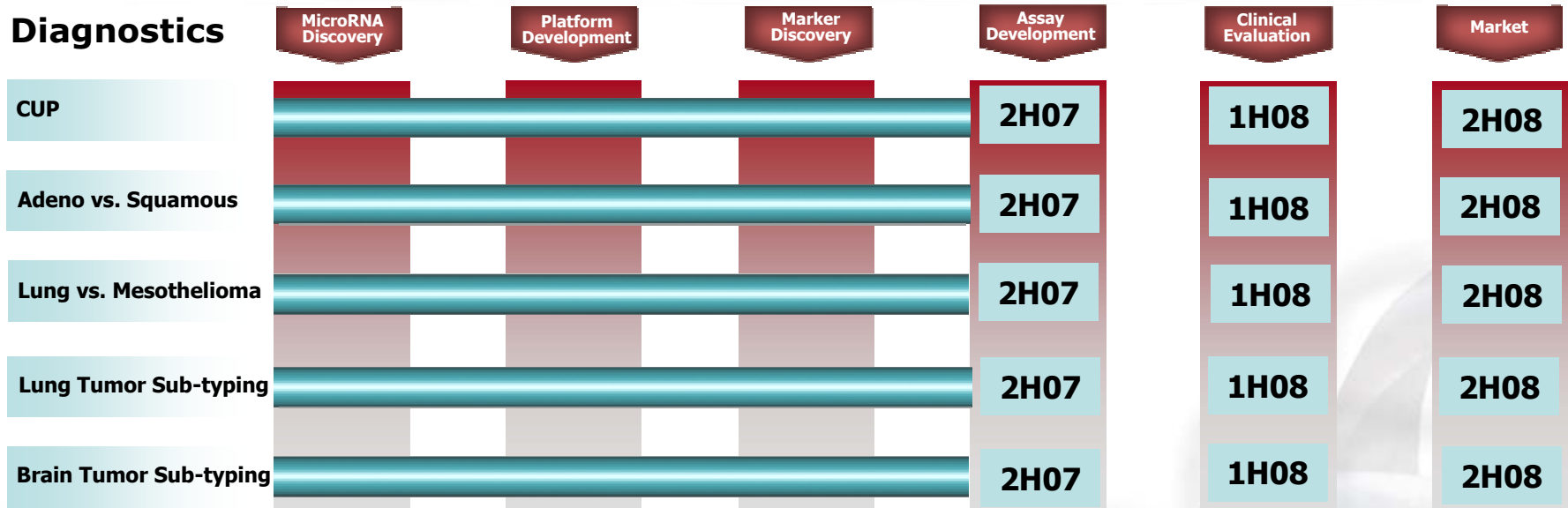
## Intellectual Property Highlights

- ◆ Rosetta has filed patents to a majority of all known human and viral microRNA
- ◆ Two USPTO microRNA Rosetta patents allowed – human (Oct '06) & viral (Jan '07)
- ◆ One allowed patent issued (May '07)
- ◆ License to allowed Tuschl microRNA patent
- ◆ Over 10 patent applications in advanced examination

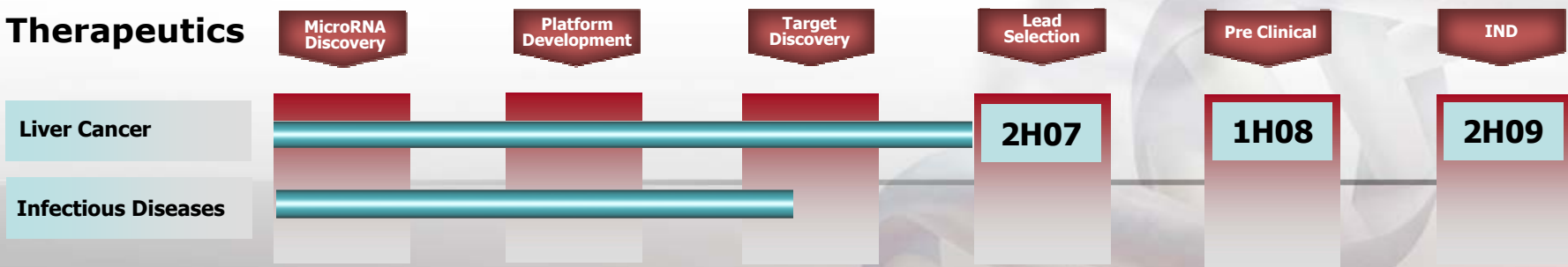


# Product Pipeline

## Diagnostics



## Therapeutics





## Financial Summary

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- ◆ Cash as of 31 March 2007 - \$36.3 MM
- ◆ Projected Use of Cash for 2007 - \$9.0 MM
- ◆ Market Cap as of 9 July 2007 - ~\$75 MM



## 2007 Objectives

- ◆ Initiate CUP Clinical Evaluation
- ◆ Complete assay development for lung and brain cancer diagnostics
- ◆ Select lead compound in Liver Cancer Therapeutics Program
- ◆ Develop additional proprietary methodologies for microRNA extraction, detection and quantification
- ◆ Establish a collaboration with a major pharmaceutical or diagnostic company
- ◆ Advance IP Estate



## Rosetta's Value Proposition

- ◆ Target Discovery Platform
  - Novel drug targets
  - Biomarker and biomarker signatures
- ◆ Cutting-edge MicroRNA Technology Platform
  - Proprietary extraction methodologies
  - Proprietary qRT-PCR and microarray systems for detection and quantification
- ◆ Multiple Commercialization Opportunities
  - Diagnostics – Rapid commercialization (2008)
  - Therapeutics – Rapid timeline from target discovery to lead identification
  - Potential Opportunities: bioenergy, cellular differentiation, cosmetics
- ◆ Dominate Intellectual Property Position

**Thank You!!**