Non-Invasive Neuromodulation: A Venture Capitalist's Perspective

Ross Jaffe, MD
Managing Director
Versant Ventures

IOM Non-Invasive Neuromodulation Workshop

March 3, 2015

VERSANT ventures

Versant Ventures at a Glance

A leading healthcare VC firm focused on biopharmaceuticals and medical devices

Experienced team of investors

- **6** Investing Managing Directors
  - **70+ years** of operating experience
  - **100+ years** of VC experience
- **6** Additional Investment Professionals with strong experience in health care

Well positioned in healthcare

- Founded in 1999, **$1.9B in capital raised**
- One of the **most active healthcare venture investors** globally
- **Strong track record** of success in medical devices and biopharmaceuticals

Global presence in medical innovation hubs

Source: VentureSource, Silicon Valley Bank

VERSANT ventures

Versant investments in neuromodulation

Company	Disease focus	Stage
Second Sight	• Blindness due to Retinitis pigmentosa	• Commercial (US/EU)
Autonomic Technologies	• Cluster headaches and migraines	• Commercial (EU)
Cerephex	• Fibromyalgia and central pain	• Clinical
Cerêve	• Insomnia	• Clinical
HOLAIRA	• COPD and asthma	• Clinical
Respicardia	• Central sleep apnea	• Clinical
Oculeve	• Dry eye	• Clinical
Metavention	• Type 2 diabetes	• Clinical
Sympara	• Hypertension	• Clinical

Venture Capitalist's Job:
Finding the Next "Big Thing"

Neuromodulation:

Exciting Convergence of Medical Science and Information Technology

- Human physiology based on electro-biochemistry
- Traditionally attacked pathophysiology with drugs or biologics
  - Historically, more known about biochemical basis of disease than electrical basis of disease
- Neuroscience illuminating electro-biochemical basis of disease
  - Nervous system modulation of other organs affects many conditions
- Advances in information technology and material sciences enabling more precise delivery of “electricity as a drug”
  - Understanding: more precise measurement of electrical as well as biochemical processes in living organisms
  - Delivery: more precise modulation of signals via a variety of energy sources – electrical, magnetic, light, acoustic, thermal

Neuromodulation:
Interesting Convergence of Devices and Drugs

	Drugs or Biologics	Traditional Devices	Neuromodulation
Anatomy			
End-organ physiology			
Cellular physiology			
Molecular physiology			

Examples

Surgery
Stents
Tissue ablation

Pacemakers
ICDs

rTMS for depression
Vagal stim. for epilepsy

Vagal stimulation for autoimmune disease

- Drugs work a molecular level to affect cells and organs
  - Challenge: drug or biologic promiscuity leads to side effects
- Traditional devices primarily modified anatomy
  - Pacemakers and ICDs do affect end-organ physiology
- Neuromodulation extends devices to cellular and molecular level

Neuromodulation:

Examples of Simple Opportunity Maps (illustrative, not comprehensive)

By Modality	Invasive	Non-invasive
Central	Deep brain stimulation Tissue ablation	rTMS TCDS
Peripheral	Nerve ablation Stimulation/Inhibition (e.g, spinal, vagal, tibial)	TENS Acoustic

By Indication		Invasive	Non-invasive
Central		Parkinson's Essential tremor	Depression Chronic Central Pain Insomnia
Peripheral	Pain	Low back pain Phantom limb pain	TENS
	Non-pain	Obesity Hypertension Autoimmune disease	Dry eye Hypertension

Medical Device Innovation in Context

You cannot have a successful medical product unless you can build a sustainable (and preferably growing) business around it

For an innovation to be come a successful medical product, you need:

- A patient who needs and wants the product
- A provider who wants to use the product
- Someone who will pay for the product
- An organization that can develop, make, and deliver the product at a profit
- Someone willing to invest resources to develop the product and build the business

If you want medical device innovation, business issues matter!

- Technical and clinical innovation is necessary, but not sufficient
- Need to analyze carefully the business issues around each opportunity

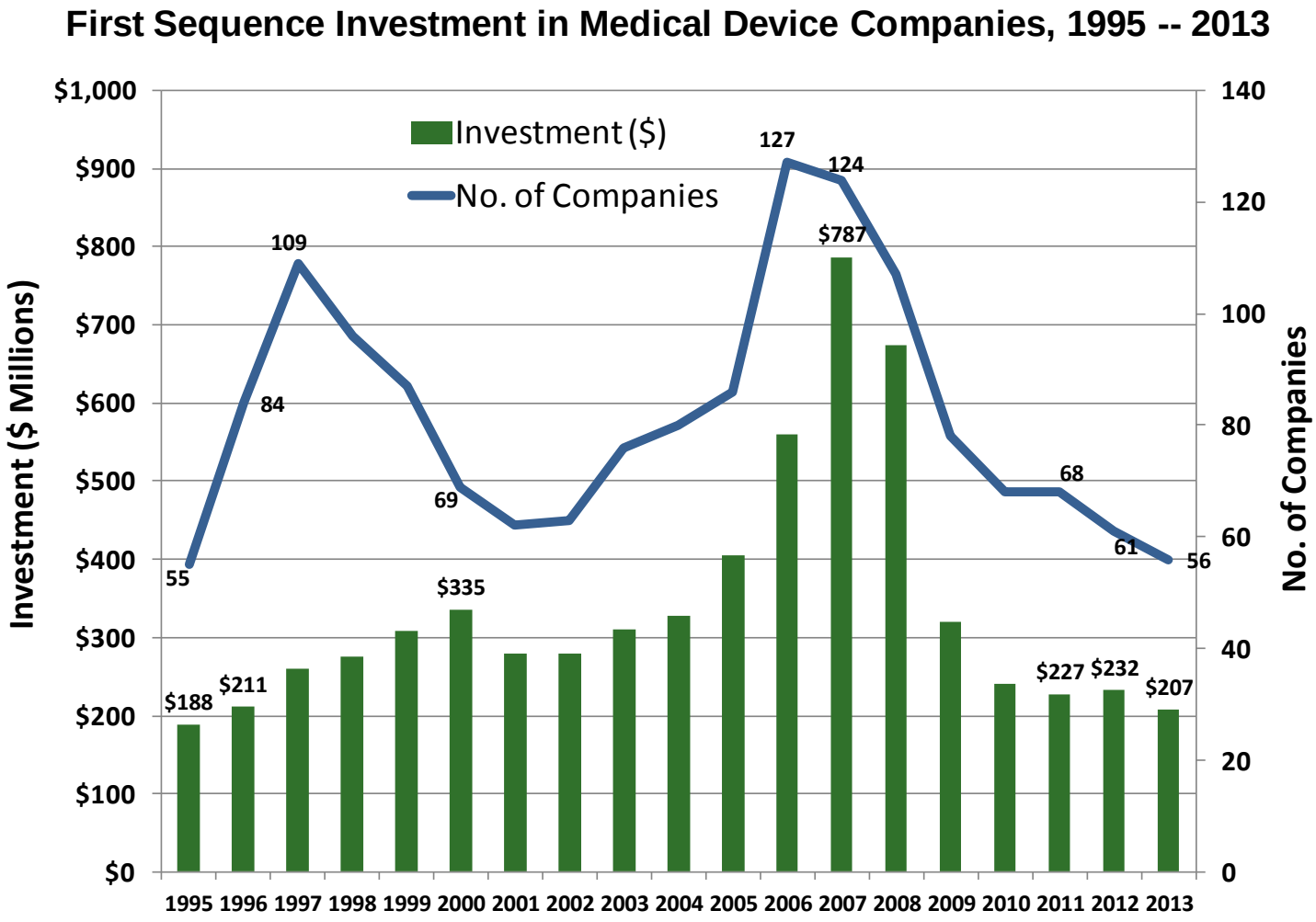
Examples of Business Issues in Neuromodulation

Both invasive and non-invasive can be attractive, but different business issues

	Issue	Invasive	Non-invasive
Market Dynamic	Rx vs. OTC	Prescription only	Rx or OTC
	Physician or Patient treatment?	Physician procedure required	Physician office treatment or patient self-use
	Product type	Permanent implant Ablation procedure	Re-usable vs. disposable Capital equipment
Regulatory	PMA vs. 510k/de novo	PMA	510k or *de novo;* none
	US or Overseas first	Often overseas first	Usually US first if low risk
Reimbursement	Patient self-pay?	No	Possible
	Need CPT code?	Yes	Yes if office procedure No if patient self use
Time/Capital	Complexity of R&D	Often complex	May be less complex
	Time to Clinical Data	Often long – need chronic data	May be faster to enroll and obtain results
	Capital Requirements	Often large	May be relatively small
Exit Options	Existing buyers?	Yes, if close to existing businesses	Fewer clear acquirers Need to prove business

The Crisis In Medtech Innovation

Start-up Investment Has Fallen >70% Since 2007



Source: PWC/NVCA Moneytree Report, 4Q2013

VERSANT ventures

Medical Device Venture Capital In 2015:
Limited Capital Available for Early-stage Investment

Longer times frames to exit reducing investment returns

- Increased time frame to exit due to FDA regulation, reimbursement
- Increased capital needs to exit -- reduces multiple on investment
- Longer time frames hurt the rate of return on investments

Many limited partner investors in VC funds pulling back from healthcare

- Other investment alternatives (e.g., buyouts) offer higher returns
- Long time to exit results in illiquidity -- limits new investment

Remaining limited partners demanding shorter time to liquidity

As a result, many health care VCs shifting to biotech and later-stage devices

- Biotech/pharma returns up given “hot” public market and acquisition activity
- Health care IT and services investment increasing given health care reform
- Early-stage medical devices less attractive: FDA, reimbursement

Non-invasive Neuromodulation:
A Time of Great Opportunity

- Exciting convergence of science and technology
  - New opportunities to use devices to treat chronic diseases
- Changing health care system demanding more cost-effective approaches to chronic diseases
- Increasing patient interest in self-treatment driving demand
  - Potential self-pay for effective non-invasive approaches
  - Opportunity for direct-to-patient distribution models
- FDA benefit-risk approach reducing regulatory barriers to neuromodulation product approval
- Emerging area of “less invasive” neuromodulation
  - Small, passive, implantable neurostim devices deliverable through minimally invasive surgery
  - Use rechargeable external devices for stimulation control

Non-invasive Neuromodulation: *A Time of Significant Challenges*

- Significant competition in some clinical areas
- Chronic conditions with subjective outcomes can make good clinical trials difficult to design and execute
- Difficult to get reimbursement for new technologies
  - CPT I code process can take several years after approval
  - Payers demanding increasing data on clinical and economic value to provide coverage and adequate reimbursement
- Early-stage capital difficult to find
  - Limited early-stage venture capital available
  - Alternative sources of capital:
    - Consider non-VC sources of investment (e.g., individual investors)
    - Use grants for R&D phase and early human data
    - Seek early corporate support
  - Need to focus on capital-efficient development

Non-invasive Neuromodulation:

“The Next Big Thing”!

VERSANT ventures