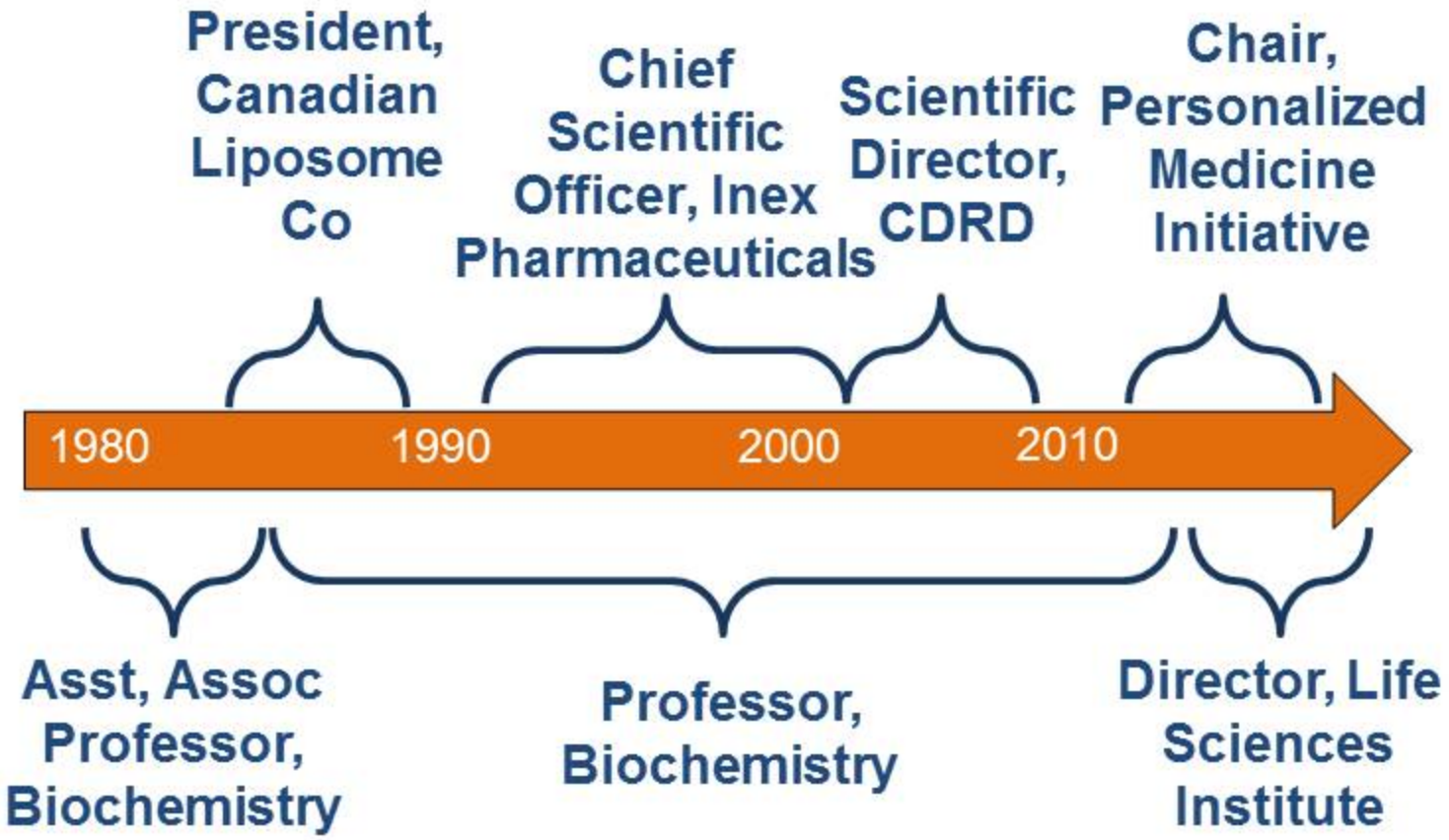
EXPERIENCES OF A SCIENTIFIC ENTREPRENEUR

- Companies and products
- Case study: Liposomal Vincristine
- The Centre for Drug Research and Development (CDRD)
- The Personalized Medicine Initiative (PMI)

Pieter Cullis
Professor, Department of Biochemistry, UBC
Director, Life Sciences Institute
Director, NanoMedicines Research Group
Chair, Personalized Medicine Initiative

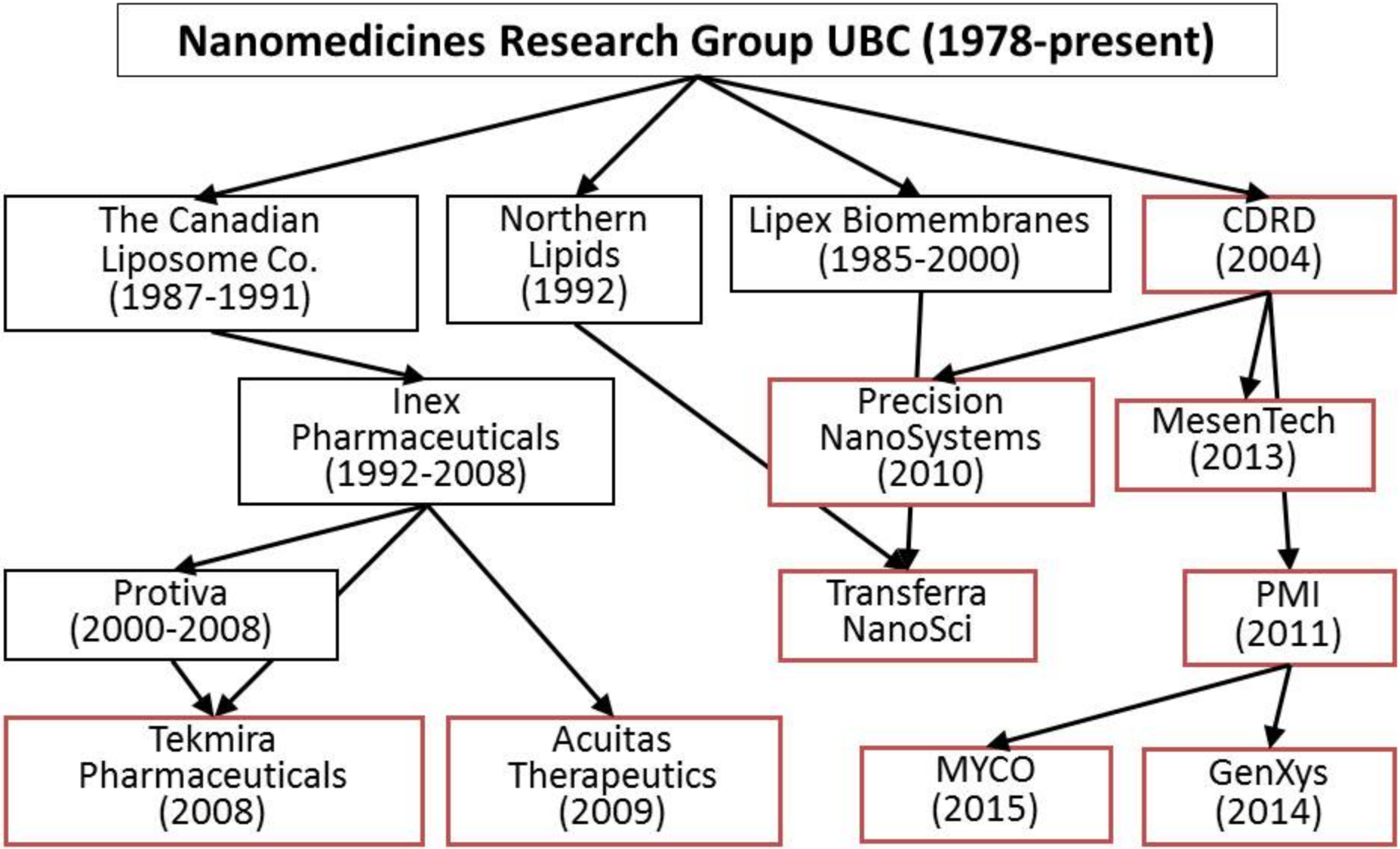
Have spent most of my career working half-time in academia and half-time in translational activities



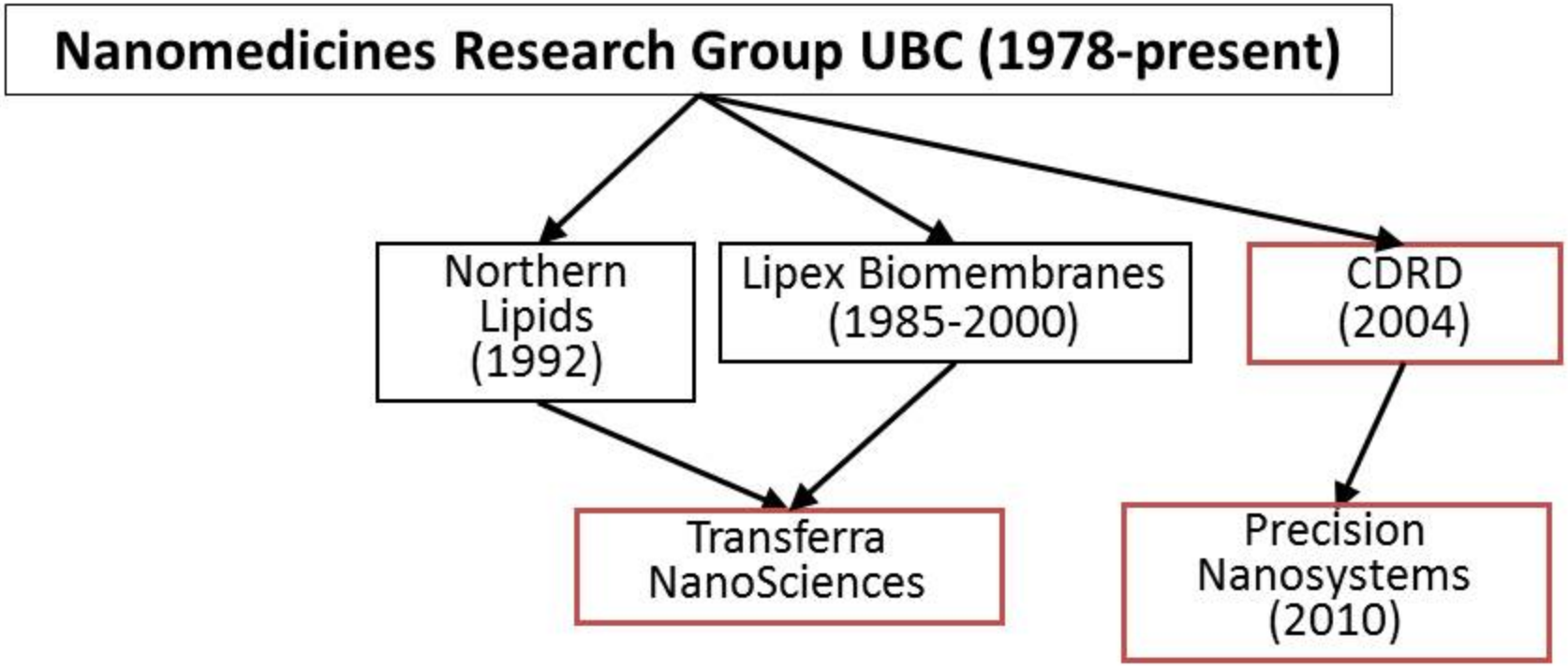
Companies Founded

1) Lipex Biomembranes Inc. (1985, now part of Northern Lipids)
2) Canadian Liposome Company Inc. (1986, incorporated into Inex (now Arbutus) Pharmaceuticals),
3) Inex (now Arbutus) Pharmaceuticals Corporation (1992-present)
4) Northern Lipids (now Transferra Nanosciences) (1991-present)
5) Centre for Drug Research and Development; CDRD (2005-present)
6) Acuitas Therapeutics (2009-present)
7) Precision NanoSystems (2010-present)
8) Personalized Medicine Initiative; PMI (2011-present)
9) Mesentech (2014-present)
10) GenXys (2014-present)
11) Molecular You Corporation (MYCO) (2015-present)

All Companies Founded Originated From My Research Group at UBC

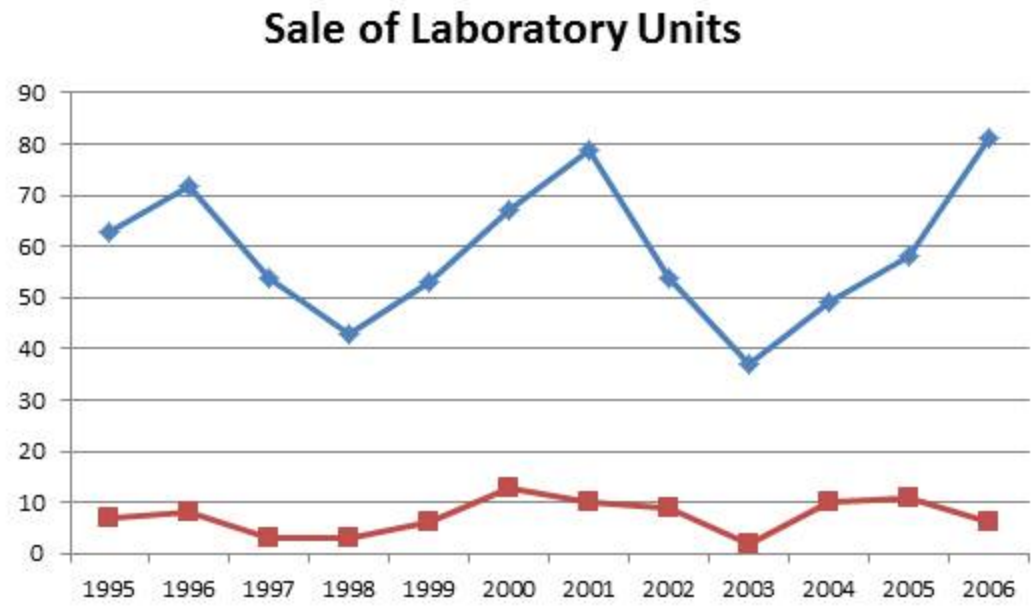


Device Companies



DEVICE	PURPOSE	STATUS	COMPANY
Extruder (1985)	LNP production	Sales > $10M	Transferra Nanosciences
NanoAssemblr (2012)	LNP production	Sales > $1M	Precision NanoSystems

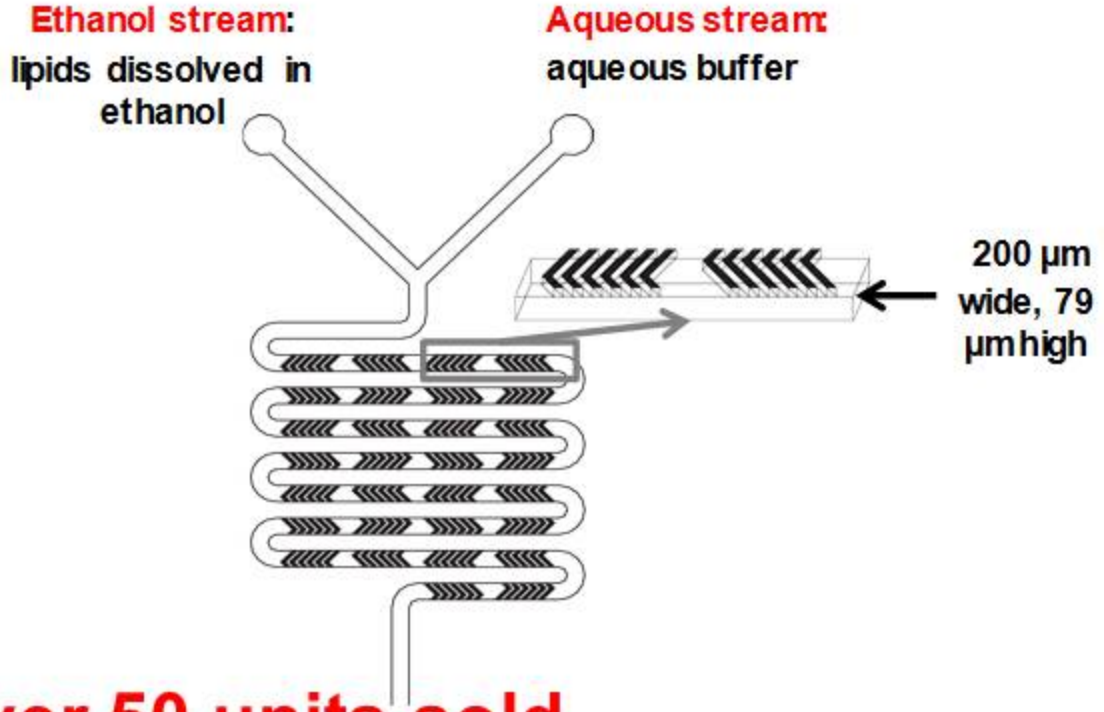
The Extruder
(now supplied by Transferra Nanosciences)



Over 2,500 units sold

Total sales 1986-2016: > $15M

The NanoAssemblr (supplied by Precision NanoSystems)



Over 50 units sold

Total sales 2013-2015: > $2M

Drug Companies

Nanomedicines Research Group UBC (1978-present)

The Canadian Liposome Co. (1987-1991)

Inex Pharmaceuticals (1992-2008)

Protiva (2000-2008)

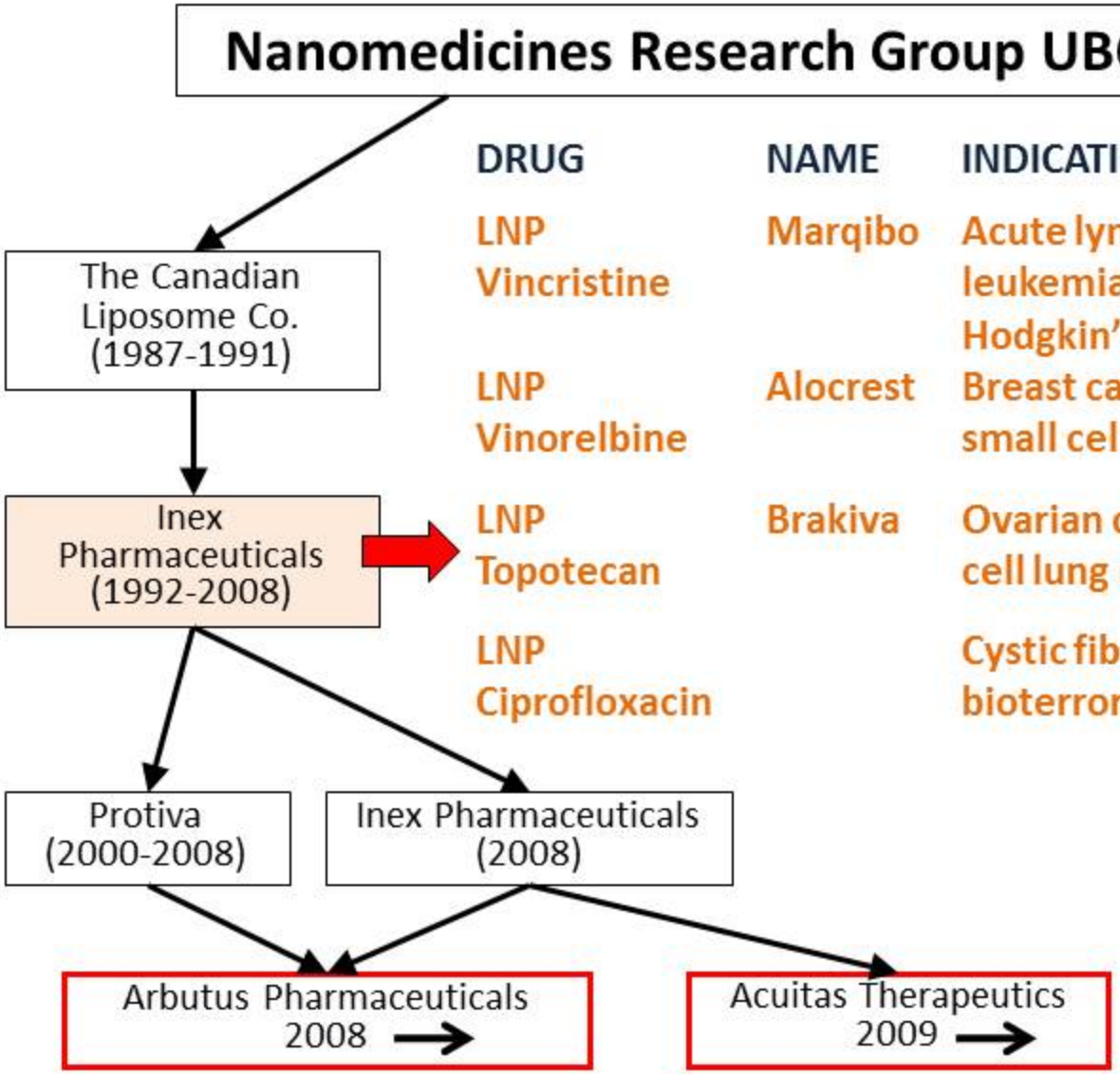
Inex Pharmaceuticals (2008)

Arbutus Pharmaceuticals 2008 →

Acuitas Therapeutics 2009 →

DRUG	NAME	INDICATION	STATUS	COMPANY
LNP Amphotericin	Abelcet	Fungal infections	Approved US 1995	Enzon
LNP Doxorubicin	Myocet	Metastatic breast cancer	Approved Europe 2000	Cephalon
LNP Vincristine	Marqibo	Leukemia	Approved US 2012	Spectrum

Drugs in Clinical Trials



DRUG	NAME	INDICATION	STATUS	COMPANY
LNP Vincristine	Marqibo	Acute lymphocytic leukemia, non-Hodgkin's lymphoma	Phase III	Talon Therapeutics
LNP Vinorelbine	Alocrest	Breast cancer, non small cell lung cancer	Phase I	Talon
LNP Topotecan	Brakiva	Ovarian cancer, small cell lung cancer	Phase I	Talon
LNP Ciprofloxacin		Cystic fibrosis, bioterrorism (anthrax)	Phase I	Aradigm

Drugs in Clinical Trials

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DRUG	INDICATION	STATUS	COMPANY
LNP siRNA (KSP,VEGF)	Primary and secondary liver cancer	Phase I	Alnylam
LNP siRNA (PLK1)	Liver cancer	Phase I	Tekmira
LNP siRNA (TTR)	Transthyretin-mediated amyloidosis	Phase III	Alnylam

Current Status

Company	Employees (approximate)
Transferra	45
Arbutus	100
CDRD	100
Acuitas	15
Precision	25
PMI	2
GenXys	6
Molecular You	4

Companies formed have led to over 4,000 person-years of employment in biotechnology in BC

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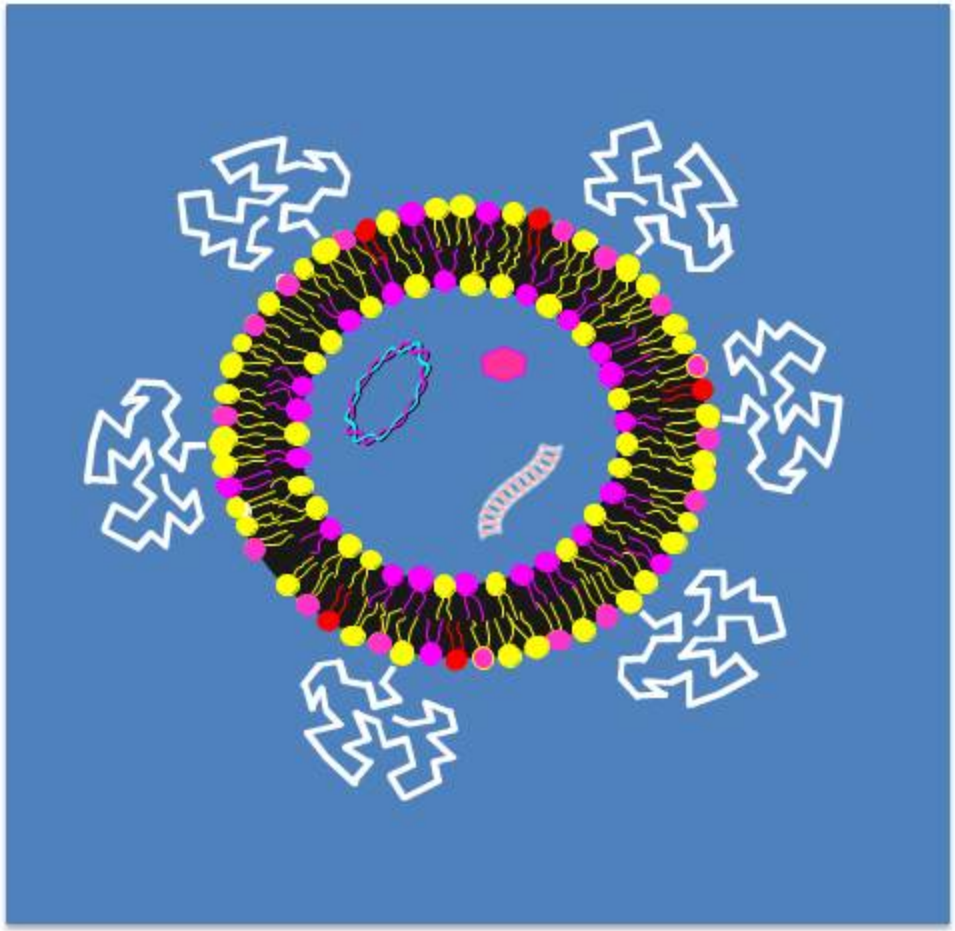
Lipid Nanoparticle Formulations



LNP Vincristine History (Marqibo)

Events in developing LNP vincristine (Marqibo)

- Developed in NanoMedicines Research Group in 1990
- Formed Inex Pharmaceuticals in 1993
- LNP vincristine entered clinical trials in 1993
- Noted activity in non-Hodgkin's lymphoma (NHL) in 1998
- Completed registration trial in NHL at 2nd or greater relapse in 2003
- Submitted to FDA for approval in 2004, approval denied
- Licensed to Talon Therapeutics (San Francisco) in 2006
- Talon completes trial in acute lymphoblastic leukemia (ALL) at 2nd or greater relapse in 2011
- Submitted to FDA for approval, positive ODAC decision March 2012, Approved August 2012!
- Licensed to Spectrum Pharmaceuticals 2013

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CDRD Addresses the Gap Between Academic Discovery and Commercialization

Academia Needs

- Funding for proof-of-concept studies to the level required for validation
- Drug development and commercialization expertise
- Specialized equipment and resources such as screening facilities and libraries
- Access to commercialization partners

cdrd

Industry Needs

- Efficient access to a pipeline of innovative early-stage technologies
- Drug candidates that have pre-clinical validation: extensive pre-clinical studies to demonstrate potential
- Technology development to be managed by industry standards
- A new model for R&D with economies of scale

Spin-Off Success

Kairos Therapeutics	Antibody-drug conjugate (ADC) platform for cancer
Sitka Biopharma	Nanoparticle platform technology for cancer
Zucara	Novel technology to prevent hypoglycemia in diabetics
Precision NanoSystems	Solutions for discovery, development and manufacture of novel nanoparticles for use as medicines and in medical research
immcure Therapeutics	Immunotherapy platforms for oncology
Mesentech	Novel technology for bone health
Sepset	Diagnostic for early and rapid diagnosis and stratification of patients likely to develop severe sepsis and organ failure

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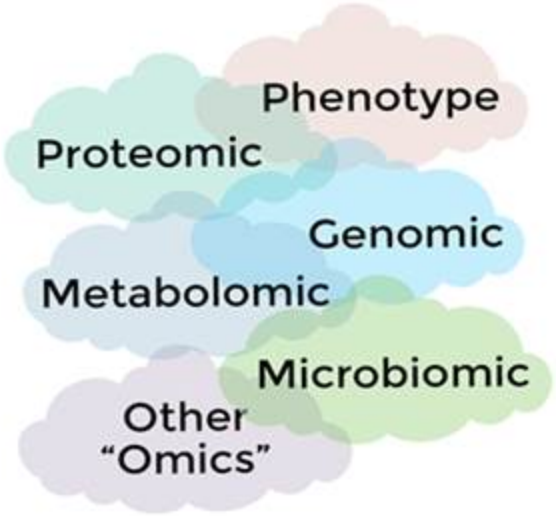
The Personalized Medicine Initiative

Vision: Introduce an individualized approach to healthcare based on the molecular makeup of the individual and their disease

Molecular "Omic" Analyses



Your Personal Molecular Data Cloud

Benefits

- Early detection of disease
- More effective and safer therapeutics
- More effective preventive medicine
- More efficient healthcare

http://personalizedmedicineinitiative.ca

PMI Objectives: Recommendations of the Roadmap

(for a copy see http://personalizedmedicineinitiative.ca/)

1. Encourage a political/public commitment to personalized medicine
2. Establish coalition of healthcare, academic, industry & patients to promote personalized medicine
3. Take advantage of near-term opportunities for implementation of personalized medicine
4. Construct a patient-centred clinical database for 25,000 Canadians

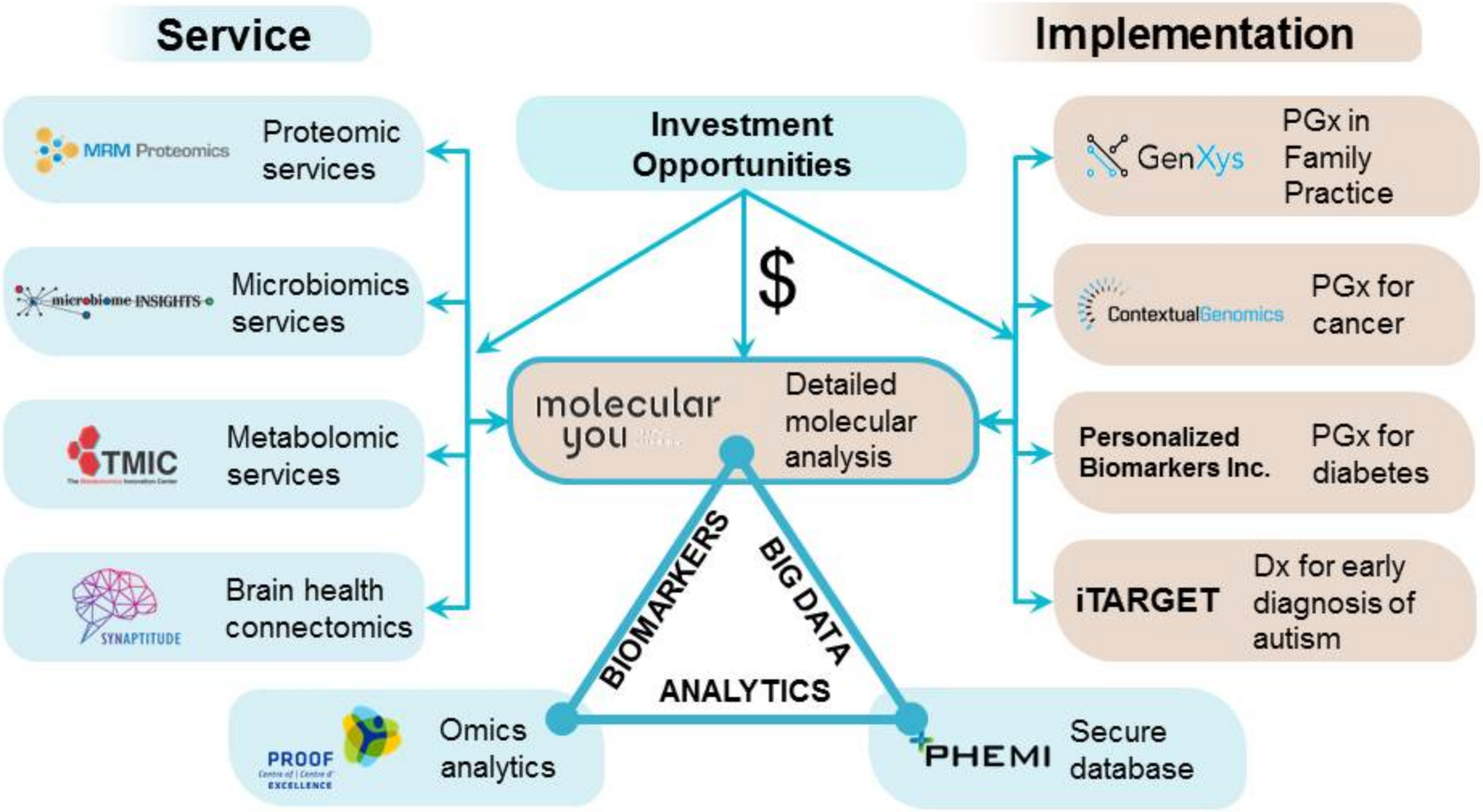
Objective 3: Take Advantage of Near-Term Opportunities

	PMI Implementation Project	Status
1	Personalized Medicine Initiative	**Operational**/ $1.5M raised
2	Pharmacogenomics in Primary Care	**Operational**/ $1.4M raised
3	Cancer genetic analyses for personalized chemotherapy	**Operational**/ $8.25M raised
4	Biomarkers for early diagnosis of autism	**Basic research**/ $1M secured
5	Biomarkers for personalized treatment of diabetes	**To be initiated**/ $100K raised
6	Microbiomic analyses	**Operational**/ $300K raised
7	Omics for preventive medicine and disease stratification	**Initiated**/ $250K raised

Commercializing Near Term Opportunities: the PMI Has Catalyzed Formation of Six Start-Ups Since 2011

1. GenXys Health Care Systems
2. Contextual Genomics
3. Cyon Therapeutics
4. Microbiome Insights
5. Personalized Biomarkers Inc
6. Molecular You Corporation

The PMI is Establishing An Ecosystem for Personalized Medicine



GenXys
Health Care Systems

GenXys; The Implementation And Evaluation Of Pharmacogenomics In Primary Care In BC

Over 65% of the patient population has a genetic variant that would change their prescription.

GenXys Addresses Basic Problems With Drug Prescription

Adverse Drug Events	Ineffective Drugs	Genetic Variations	Medication Selection
4th leading cause of death	60% of prescribed drugs do NOT benefit the individual	97% of the population has at least 1 actionable genotype	Genetics is only 1 element of the complex drug selection process

Genetic guidance is contained in package insert for > 150 drugs, but never used in family practice

GenXys is Constructing Algorithms to Assist in Making Best Prescription

Algorithms written using the highest levels of evidence using:

- Patient characteristics; age, gender etc
- Co-morbidities
- Drug-drug interactions
- Drug side effects
- Pharmacogenetic interactions
- Drug costs

Financial Impact in Healthcare

Implementation of GenXys would save Canada >$1 Billion per year in hospitalizations and ER Visits

- Dionne and Mitton

ER visits decline 71% hospitalizations 39%

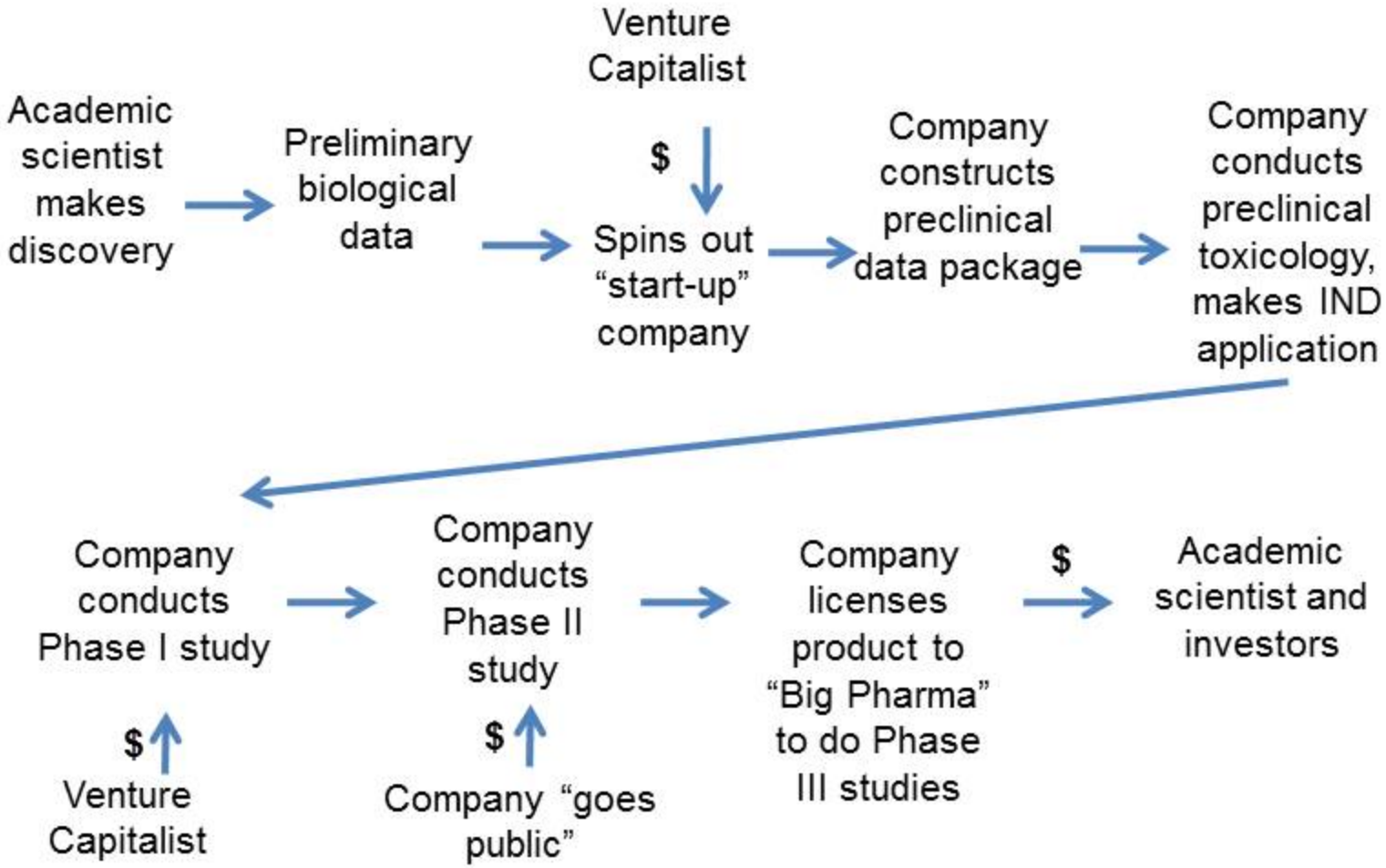
- Journal of Medical Economics (2015)

GenXys

Models For Founding Companies From Academia

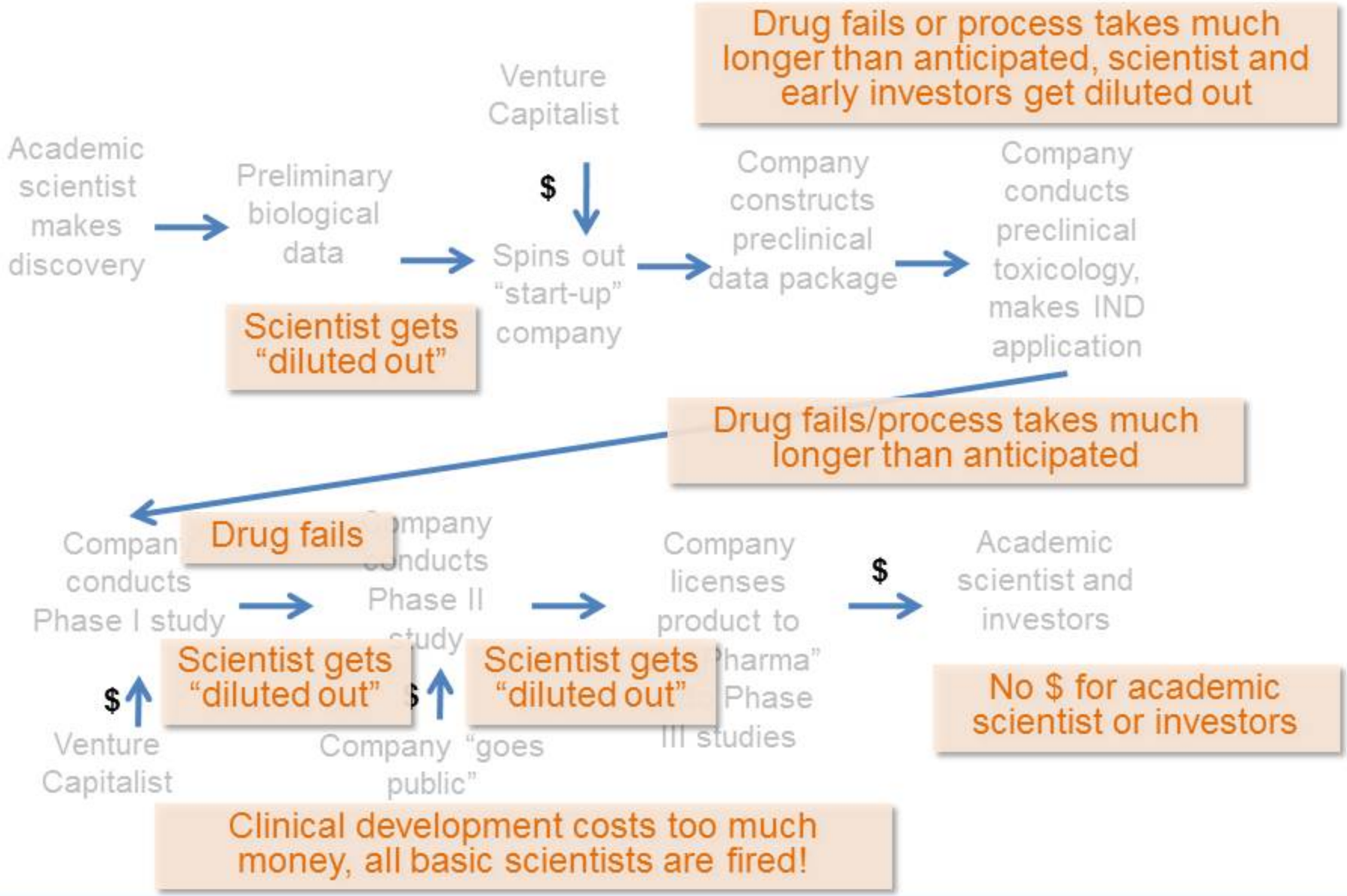
1) The Inex (now Arbutus) model
2) The CDRD model
3) The Precision NanoSystems model
4) The PMI model

The Inex (now Arbutus) Model



It never happens this way any more!

The Usual Results of the "Classical" Scientific Entrepreneur Process



CDRD Develops Comprehensive Technology Dossiers on Candidate Drugs to Enhance Commercialization Prospects

A sophisticated and complete pre-clinical Technology Dossier is required to justify the large investment needed to move a drug into clinical trials:

- Mechanism of action (target identification and validation)
- Lead identification (screening)
- Lead optimization (medicinal chemistry)
- Drug formulation and drug delivery systems/processes
- Absorption, distribution, metabolism and excretion (ADME) studies
- Pharmacokinetic and biodistribution properties
- Comprehensive efficacy and toxicity studies
- Intellectual property
- Clinical strategy and likelihood of clinical success
- Manufacturing issues, market issues, etc.

The Precision NanoSystems Model

- Invent new technology in lab
- Convince University-Industry Office to patent it (or patent yourself)
- Form company ("NewCo") and raise seed funds
- License patent from University into NewCo
- Put research contract in place between NewCo and lab (all improvements flow to company)
- Write grants for translational funds to move NewCo products forward
- Move NewCo out of lab when products are mature enough to secure outside funding

The Personalized Medicine Initiative Model

Moving molecularly-based medicine into the front lines of healthcare

- Identify opportunity e.g. pharmacogenomics
- Establish collaboration between basic Life Science researcher and clinician
- Develop diagnostic test to be implemented into healthcare
- Identify patient cohort and apply for funding to implement test in patient cohort
- Establish a company to commercialize the diagnostic
- NewCo raises money to streamline the test and move into the population

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- Assemble a team and keep it together!

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Norbert Maurer

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PMI

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