Managing Intellectual Property to Optimize the Impact of Academic Research on Global Health

Annual Intellectual Property Symposium

Franklin Pierce Law Center

April 23, 2010

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Boston University

Agenda

- The role of public sector in drug discovery
- The importance of academic licensing policies
- The pharmaceutical industry from 35,000 feet
- Ways to encourage affordability
- Where are we today?

University Licensing Policies and Global Health

- Problem first surfaced in 2001 with Yale and Zerit
- d4T discovered by Drs. Tai-Shun Lin and William Prusoff
- Funded by NIH and Bristol-Myers
- Exclusively optioned then licensed to Bristol-Myers
- On list of Essential Medicines developed by *Medécins Sans Frontieres*
- Requested waiver of S. African patent
- Yale said they were powerless – BMS had an exclusive license

The Zerit/Yale Story

- Enter Amy Kapczynski 

- First year Yale Law Student
- Had met Toby at an AIDS conference in Durban in July 2000
- Toby identified that Yale held the patent and contacted Amy
- She secured support of Prusoff and Michael Merson, Dean of Yale's School of Public Health
  - Former head of WHO HIV/AIDS program

Yale Pressed to Help Cut Drug Costs in Africa

By DONALD G. McNEIL Jr.
Published: March 12, 2001

PARIS, March 11— Trying a new tack to drive down the price of AIDS medicines, the medical charity Doctors Without Borders has asked Yale University to permit South Africa to import a generic version of a drug on which Yale holds the patent.

The university, citing a patent contract with Bristol-Myers Squibb, has refused. But the Yale press office released a brief statement on Friday saying Yale had removed all barriers to Bristol-Myers in making the drug readily available in South Africa and hoped it would do so.

A group of Yale law students, distressed that their university looks complicit in keeping the drug out of reach of thousands of dying South Africans while getting $40 million a year in license fees, have been planning to pressure Yale.

A Bristol-Myers spokesman said the company was planning action because of the Yale protest, but declined to describe it.

The drug in question is d4T, an antiretroviral drug also known as stavudine or by the brand name Zerit. It was one of the first components of the triple-therapy AIDS cocktail

Maker Yielding Patent in Africa For AIDS Drug

By MELODY PETERSEN and DONALD G. McNEIL Jr.
Published: March 15, 2001

Bristol-Myers Squibb said yesterday that it would no longer try to stop generic-drug makers from selling low-cost versions of one of its H.I.V. drugs in Africa, making it the second drug company in a week to greatly change its policies in the face of the AIDS epidemic.

It is extremely rare for a drug maker to yield its rights over a patent, which gives it a monopoly in selling a drug. But the AIDS crisis has subjected the industry to critiism that its prices are keeping millions of poor people in Africa from getting vital care.

Bristol-Myers holds the patent on a drug known as d4T or stavudine, which is sold under the brand name Zerit, and said it would not use its legal rights to keep lower-cost generic versions of this drug out of South Africa or any other African nation.

Yale University, which owns the rights to the Zerit patent with Bristol-Myers, said it would go along.

Bristol-Myers, based in Manhattan, also said it would sharply reduce the price of Zerit and another AIDS drug, ddI or didanosine, which is sold as Videx, in Africa, to a combined price of $1 a day. The company does not own the patent to Videx.

In the United States, by contrast, one day's dose of the two drugs costs $18, the company said.

Bristol-Myers's announcement goes beyond sharp price cuts taken last week by Merck &

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Was Zerit an isolated case?

Academia and Drug Discovery

- Traditional roles:
  - Public sector scientists, with public funding, elucidate disease mechanisms and identify promising points of intervention
    - — i.e., Basic Research
  - Private sector scientists, with private funding, use this knowledge to identify, test and clinically develop new drugs and vaccines
    - —i.e., Applied Research

Then the Roles Changed

1975 - 1980

- Basic tools of biotechnology developed – monoclonal antibodies and recombinant DNA
- Passage of the Bayh-Dole and Stevenson-Wydler Acts

1980 - present

- A significant number of drugs and vaccines have been discovered by public sector scientists, patented, licensed and gone on to receive FDA approval

Criteria for Inclusion

- Products which have received FDA approval by either:
  - Center for Drug Evaluation and Research (CDER) or
  - Center for Biologics Evaluation and Research (CBER)
- A license to intellectual property was signed (or enforced by the Courts)
- US Public Sector Research Institutions only
  - National Laboratories
  - Universities
  - Hospitals
  - Non-profit Research Institutes
- Each BLA/NDA resulting from that IP

Criteria for Inclusion

- Includes:
  - Vaccines
  - Small molecule drugs
  - Biologics
  - *In vivo* diagnostics
- Excludes:
  - Platform technologies that contribute to the development of whole classes of drugs
    - Cabilly
    - Axel
    - etc.
  - Nutritionals

Sources for Study

Primary:

- FDA – Orange Book, CDER and CBER databases
- SEC – EDGAR database
- ReCap / ReCapIP
- USPTO
- CRISP
- iEdison

Secondary:

- AUTM Surveys (e.g. Better World Report)
- University of Virginia Patent Foundation research
- Press articles
- Lawsuits
- Personal communications, etc.

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Results

Number of Products

Type of Product	Number
New Chemical Entity	93
Biologic	36
Vaccine	15
Over the counter	1
In-vivo diagnostic	8
Total	153*

* After data collection was completed, the FDA approved Folotyn , which was discovered by SRI International, Southern Research Institute and Sloan-Kettering, and is licensed to Allos Therapeutics

Therapeutic Categories

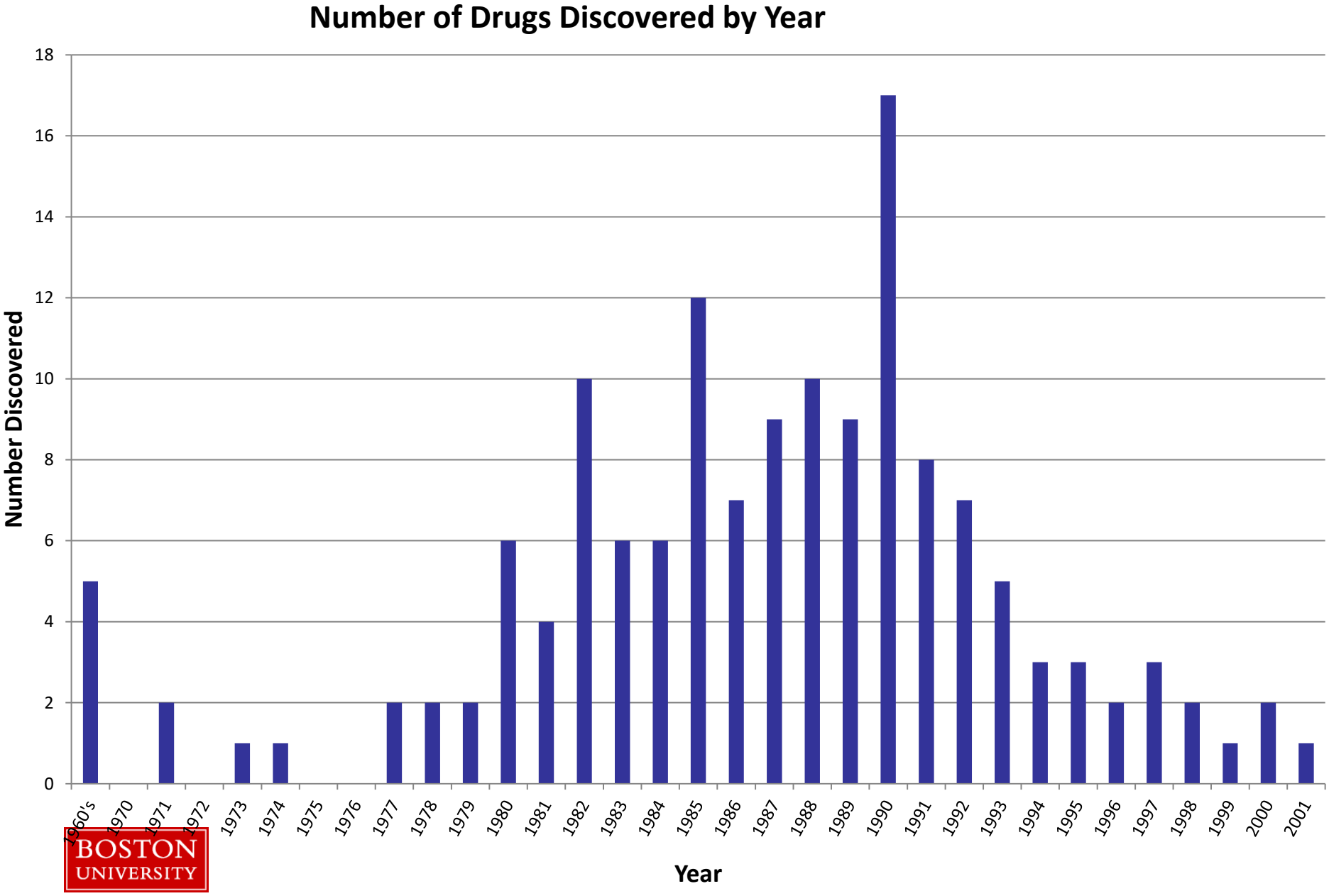
Therapeutic Area	Number
Hematology/Oncology	40
Infectious Disease	36
Cardiology	12
Metabolic	12
CNS	12
Dermatology	7
Renal	7
Ophthalmology	6
Immunology	6
Gastroenterology	4
Women's Health	3
Allergy	2
Pulmonary	2
Urology	2
Anaesthesiology	1
Dental	1
	153

Discovering Institution	Number
National Institutes of Health	22
U. of California	11
Sloan Kettering	8
Emory University	7
Yale University	6
Children's Hospital, Boston	5
MIT	5
Salk Institute	5
Wisconsin Alumni Research Foundation	5
Columbia University	4
New York University	4
U. of Michigan	4
U. of Minnesota	4
U. of Texas	4
Brigham & Women's	3
Dana-Farber Cancer Institute	3
Harvard	3
Massachusetts General Hospital	3
Oklahoma Medical Research Foundation	3
Rockefeller University	3
Scripps	3
State University of New York	3
Tulane University	3
U. of Cincinnati	3

Initial Developers

Type of Entity	Number	%
Large Entity	65	42.5%
Small Entity	65	42.5%
Start-Up	23	15.0%
Total	153	

Current Marketer	Number
GlaxoSmithKline	12
J&J	9
Bristol-Myers Squibb	8
Merck	8
Pfizer	8
Eli Lilly	6
Genzyme	6
Novartis	6
AstraZeneca	5
Wyeth	5
Amgen	4
Bayer Healthcare	4
Eisai	4
Roche	3
Abbott	3
Baxter Healthcare	3
BiogenIdec	3


Number of Drugs Discovered by Year
Number Discovered
0
2
4
6
8
10
12
14
16
18
1960's
1970
1971
1972
1973
1974
1975
1976
1977
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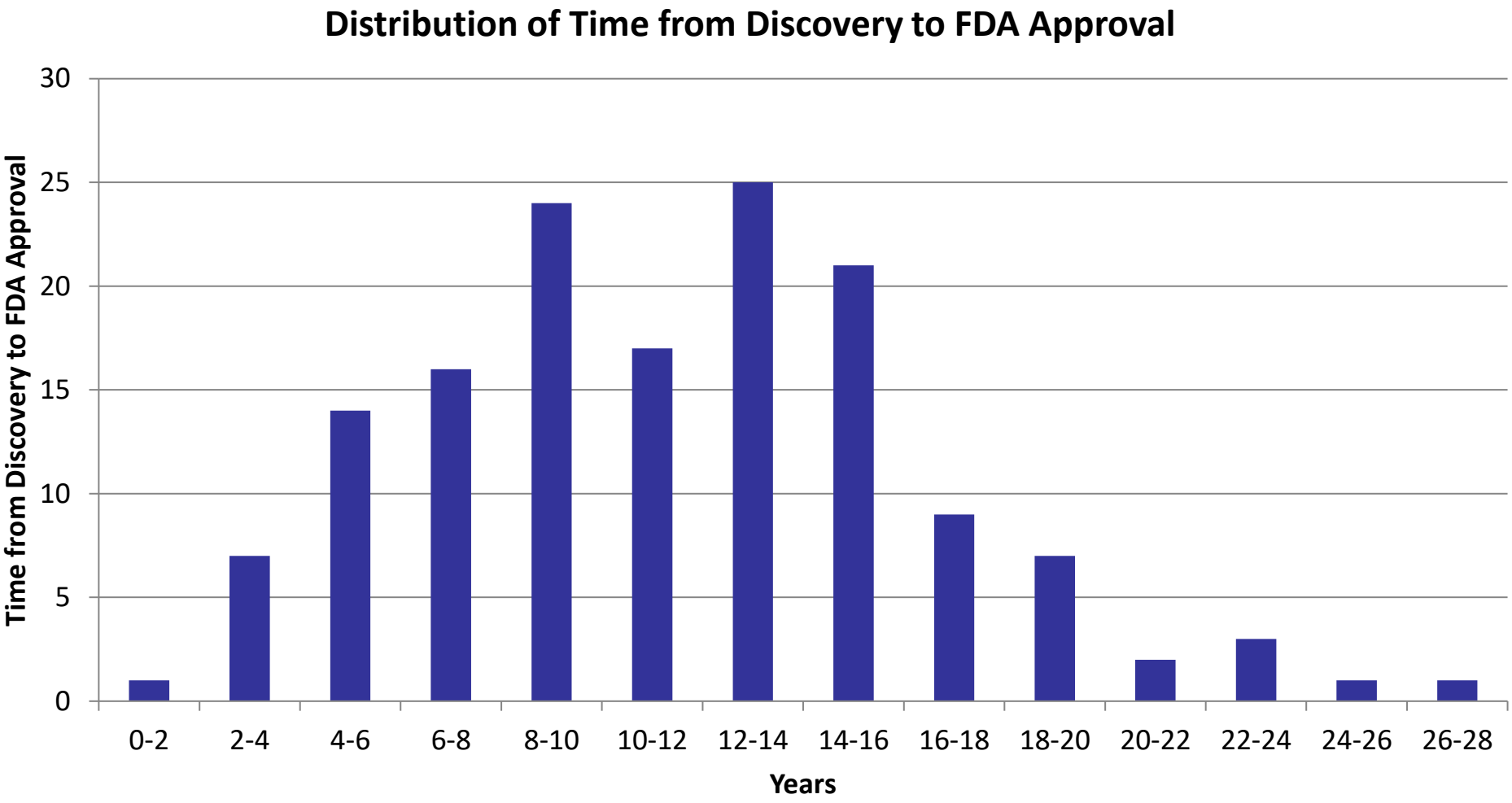
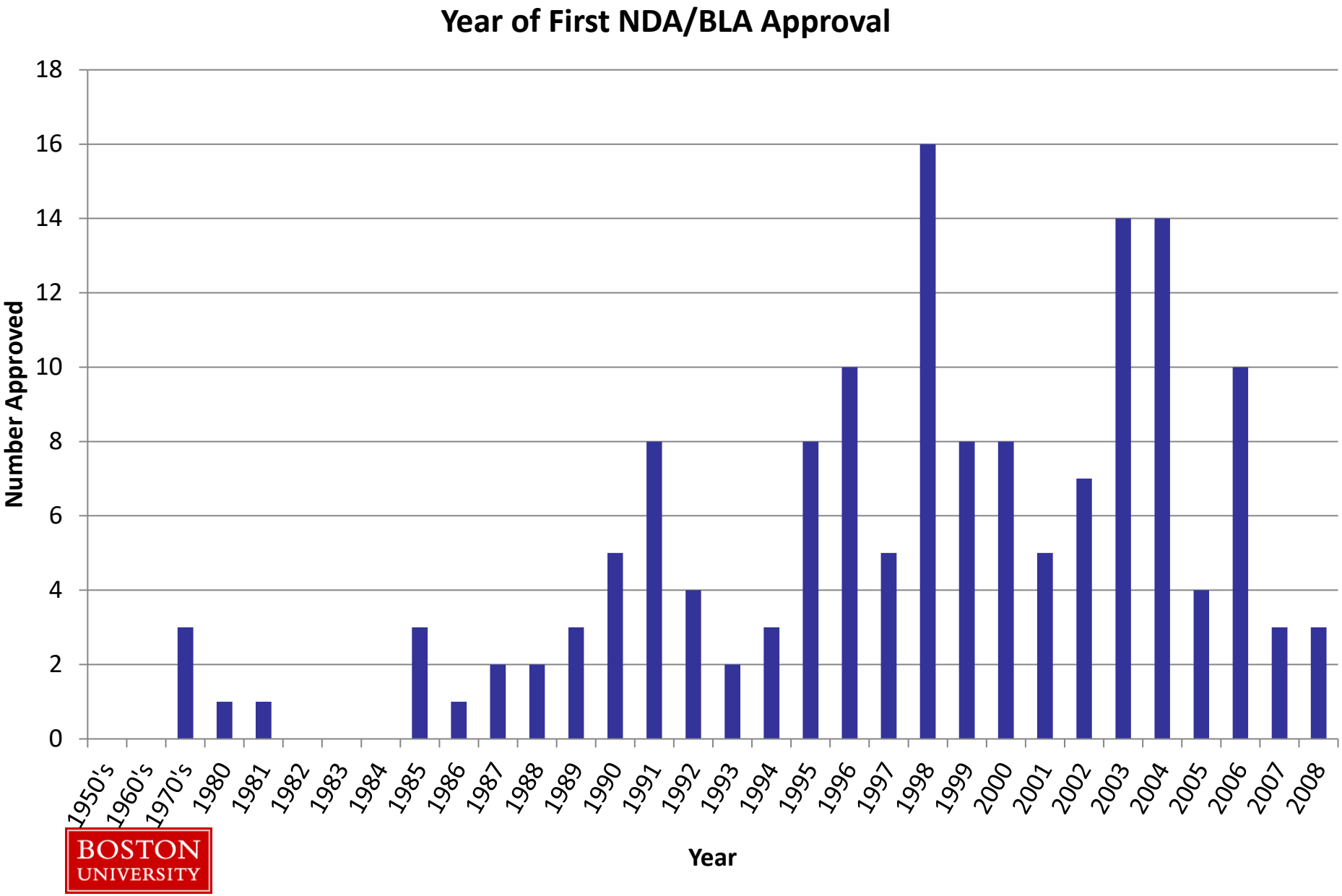
Year


Distribution of Time from Discovery to FDA Approval
Time from Discovery to FDA Approval
30
25
20
15
10
5
0
0-2
2-4
4-6
6-8
8-10
10-12
12-14
14-16
16-18
18-20
20-22
22-24
24-26
26-28
Years


Year of First NDA/BLA Approval
Number Approved
0
2
4
6
8
10
12
14
16
18
1950's
1960's
1970's
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
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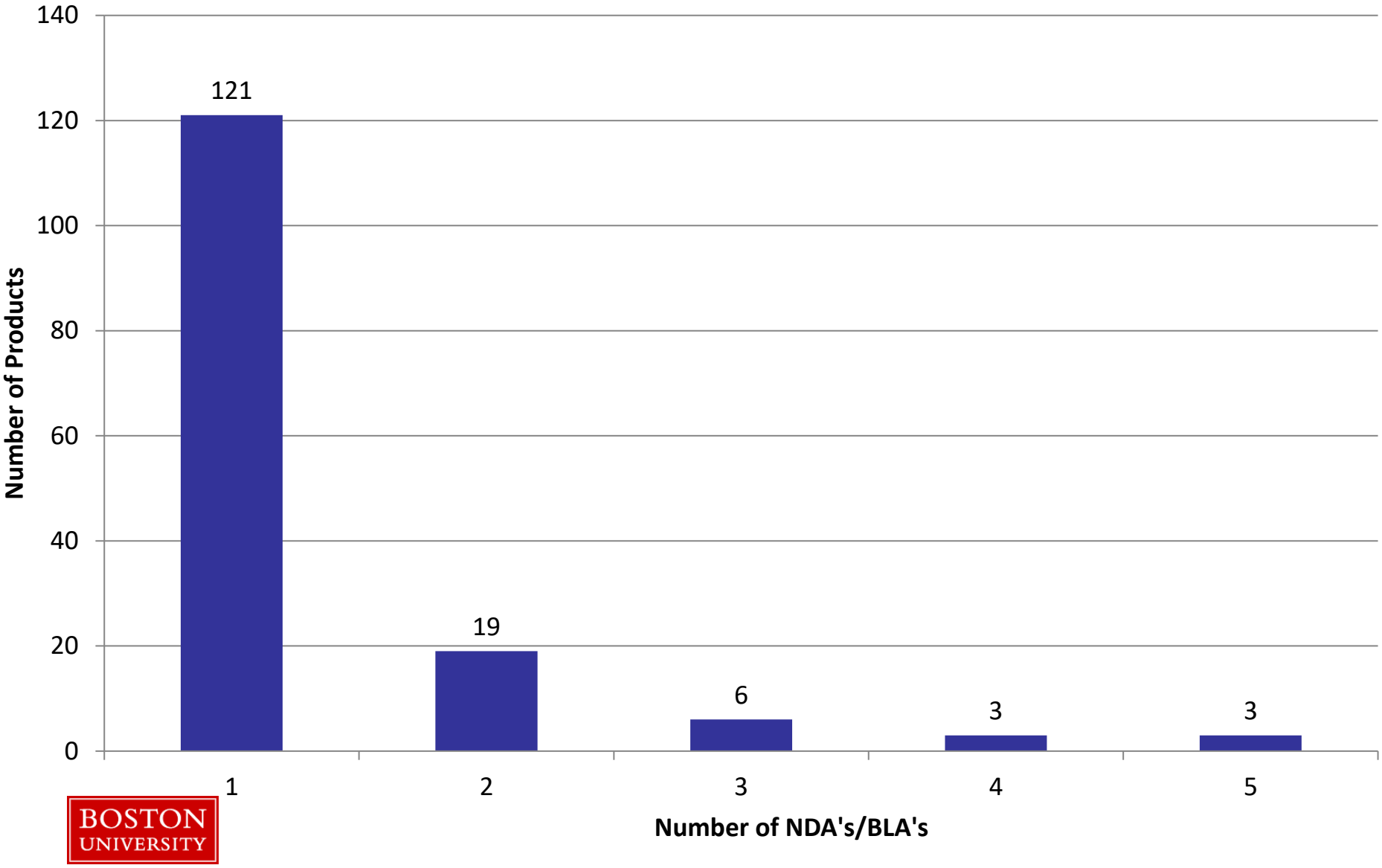
2003
2004
2005
2006
2007
2008
Year

Figure 6: Number of NDAs/BLAs per Product



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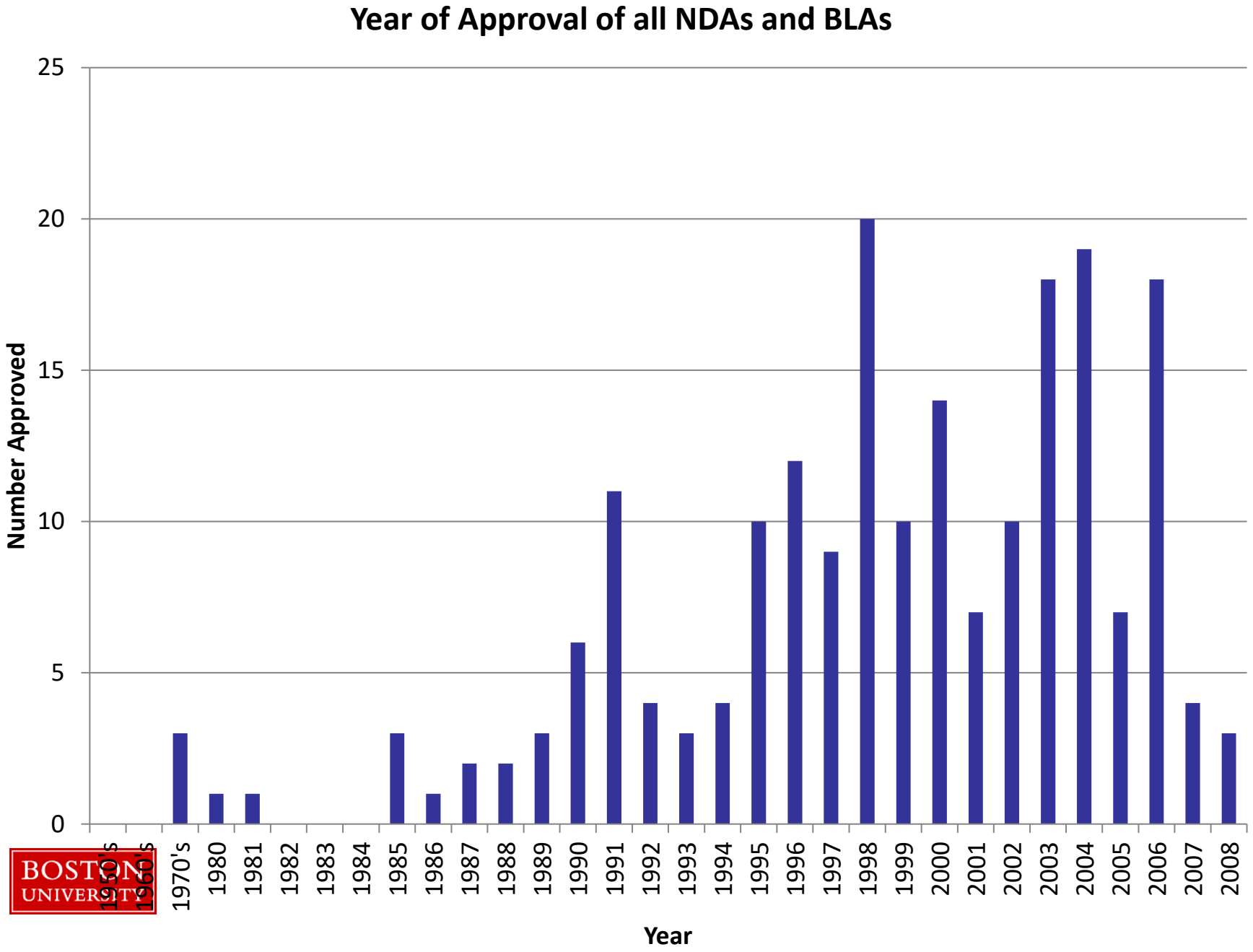
Year of Approval of all NDAs and BLAs
Number Approved
25
20
15
10
5
0
1950's
1960's
1970's
1980
1981
1982
1983
1984
1985
1986
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1988
1989
1990
1991
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2007
2008
Year

Therapeutic Impact

- Two measures of therapeutic impact by FDA
  - Chemical type
    - NME to OTC switch
  - Type of review
    - Standard vs. Priority
- Highest therapeutic impact = NME with Priority review

Therapeutic Impact (1990-2007)

	Total	Public Sector	%
NDA Approvals	1,541	143	9.3%
NME Approvals	483	64	13.3%
Priority Reviews	348	66	19.0%
NME Priority Reviews	209	44	21.1%

Commercialization Pathways

- Found that the classical models for commercialization of public sector research:

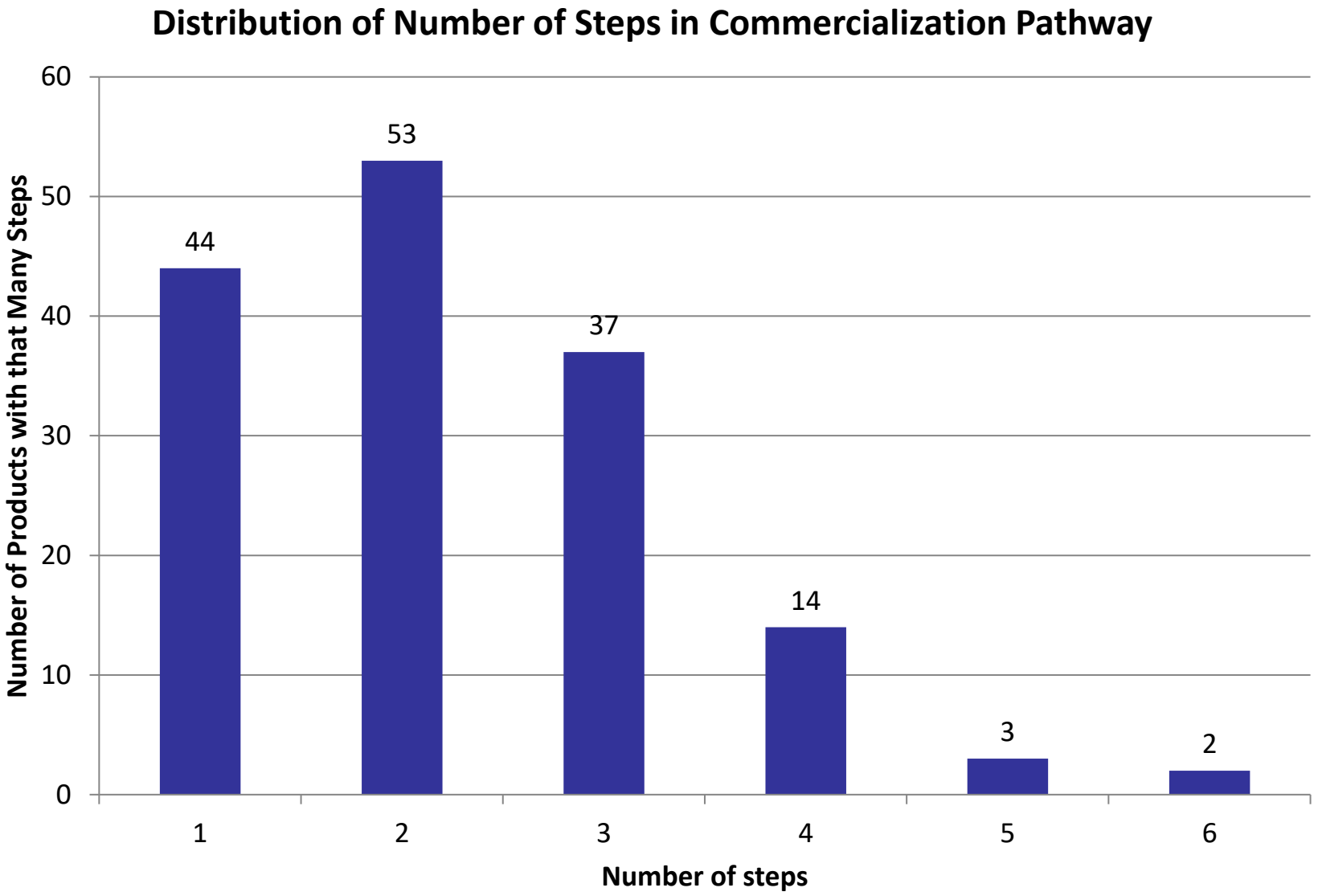
PSRI → Large Pharma → Market

and

PSRI → Biotech → Large Pharma → Market

are considerable over-simplifications

- There are frequently one or more additional transactions both pre- and post-FDA approval.



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Commercialization Pathway vs. Initial Developer

No. of Steps	1	2	3	4	5	6
Large Entity	39	14	10	1	1	0
Small Entity	4	31	18	10	1	1
Start-Up	1	8	9	3	1	1

Macugen

- Initial patent filed by U. of Colorado, June 1990
- Licensed to NeXstar, $1 million in stock and research, June 1991
- NeXstar acquired by Gilead $550 million in stock, March1999
- Gilead sublicensed rights to Eyetech, $32 million, April 2000
- Eyetech partnered with Pfizer $760 million, December 2002
- FDA approved Macugen, December 2004
- U. of Colorado monetized part of its royalty interest for $45 million (est) Jan 2005
- Eyetech acquired by OSI Pharmaceuticals $935 million, August 2005

Marketer

- 36 Orphan drugs
- 21 products no longer sold
- >$1 billion global 28
- >$1 billion US 12
- >$8 billion 3

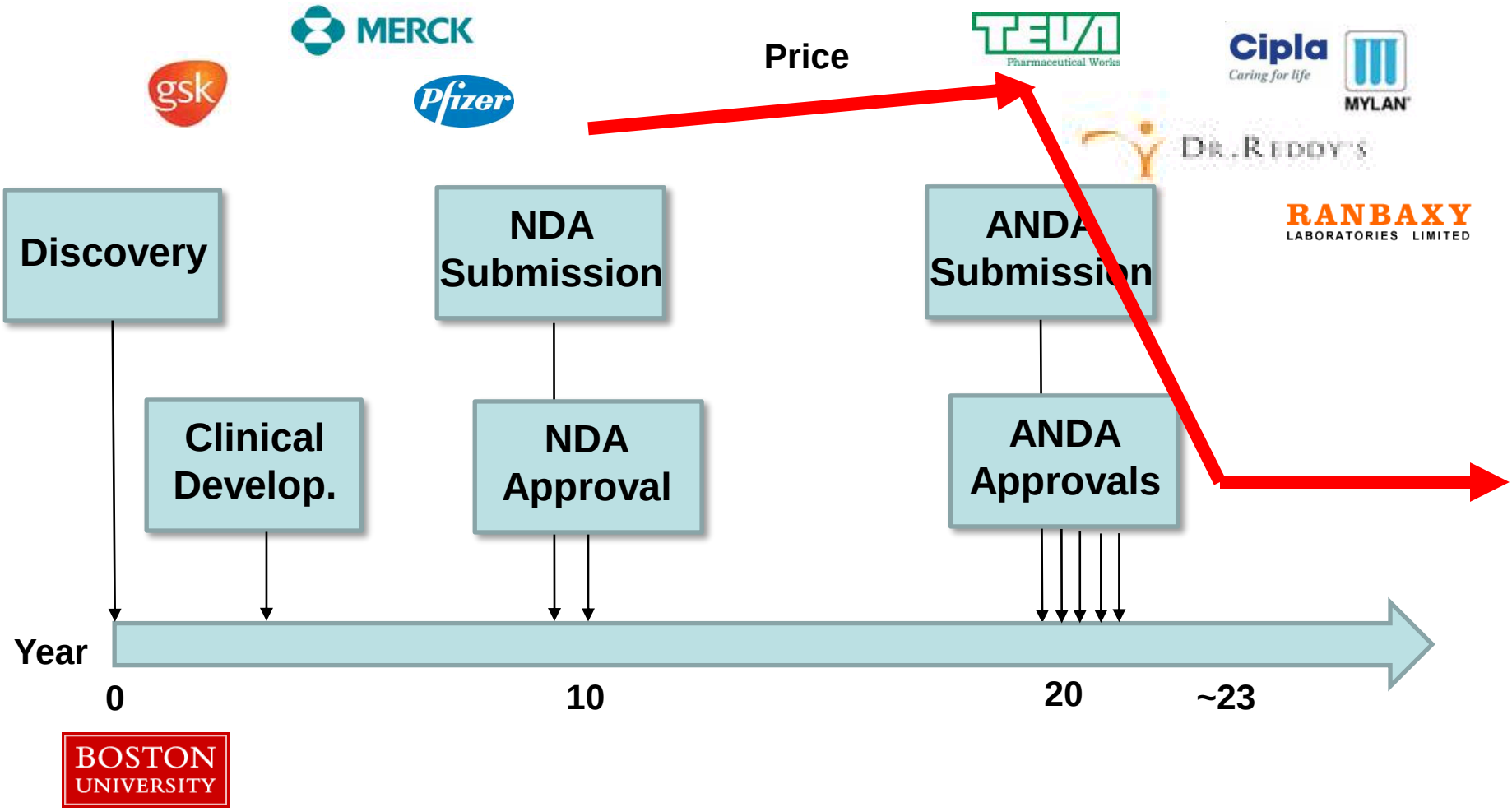
Source: IMS Health

Conclusions

- Public sector research institutions play an important role in discovering new drugs
- Their licensing policies will significantly impact avaialbility and affordability in the developing world

The Pharmaceutical Industry from 35,000 feet

How the Pharmaceutical Industry Works



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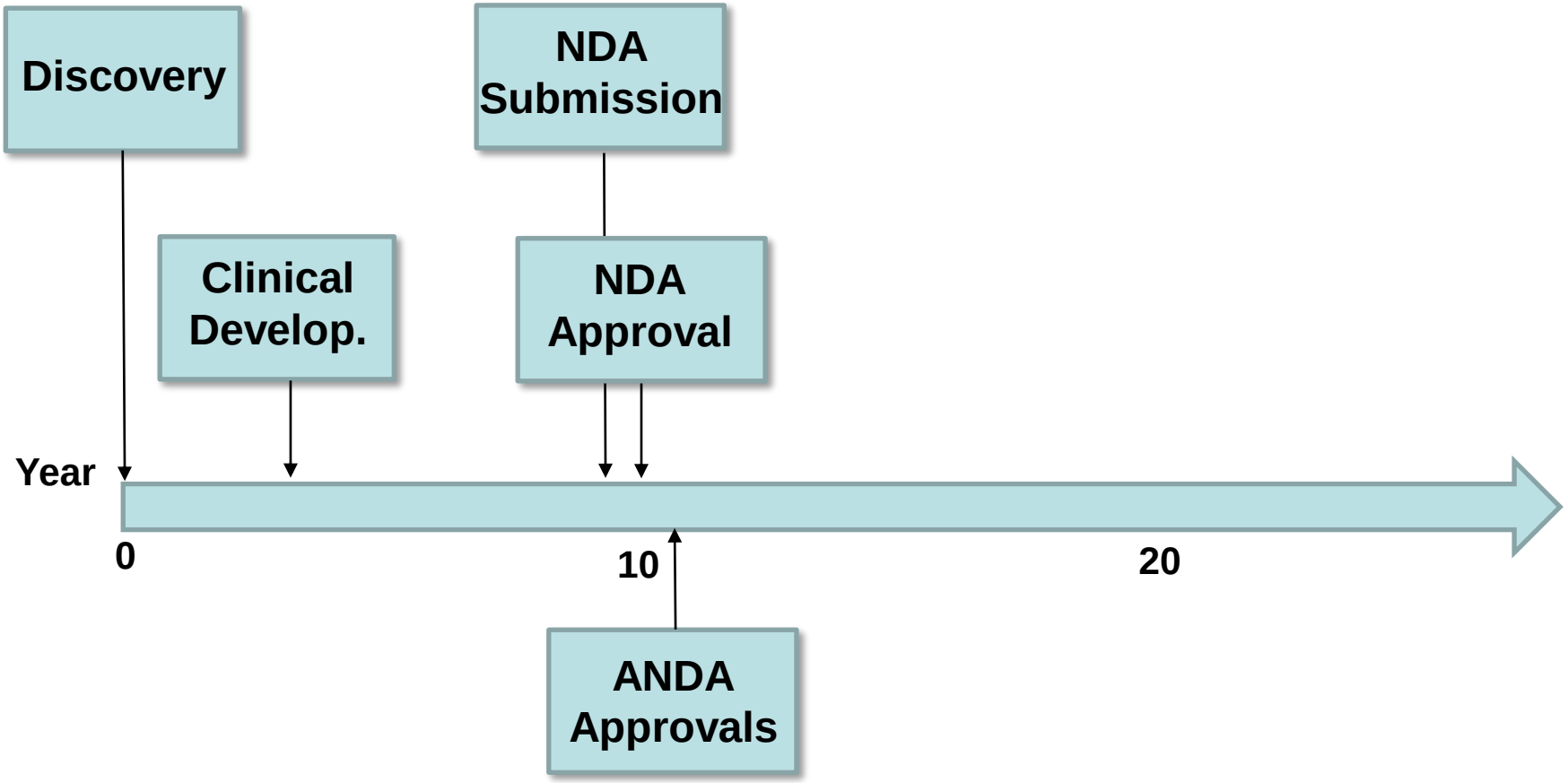
The New Pharmaceutical Paradigm



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Cipla Caring for life

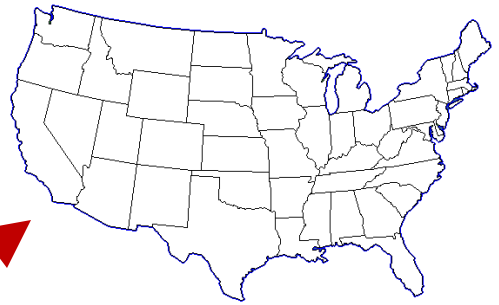
RANBAXY LABORATORIES LIMITED

DR. REDDY'S

How do we achieve this?

- We could try to change the patent system to achieve this
- Or we could change the licensing system
- The problem isn't the patent system
  - Patents just give you control over what happens to your IP
  - An essential component of the innovation system
  - We should be very cautious about changing it
- It's much easier (and less risky!) to change licensing behavior
  - E.g. PCT Treaty signed 1970
    - Came into effect in 1978
  - Treaty of London (EPO issuances) signed 2000
    - Came into effect 2008

Let's think about how we get a public sector discovered drug to the global market



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The Traditional Academic Development Model

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How could we modify this process to achieve affordability?

Include Developing Country Milestone and Pricing

Licensee shall seek registration in a developing country by…….

Licensee shall make available in developing countries at prices no more than 50% more than fully burdened manufacturing cost

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Don't Allow Patenting in Developing Countries

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Separate Licensees

MERCK

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Mandatory Sublicensing

MERCK

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Non-Assert

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Managing Intellectua

les Nouvelles

JOURNAL OF THE LICENSING EXECUTIVES SOCIETY INTERNATIONAL

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LES

Where are we today?

The Issues

- Academic technologies are embryonic, high risk and uncertain
  - "A hot academic technology is one that two companies are interested in"
  - "First do no harm"
- Where is the motivation for Universities to include global health protections?
  - Makes the negotiation more difficult
    - Potential show stopper
  - Reduces income (maybe)
  - Rarely any incentive compensation to motivate Licensing Managers
  - Part of academic social mission
  - Culture of academic licensing
- Power lies with corporate licensees
  - Gilead, Glaxo, J&J, Merck in leadership position on voluntary licensing
  - What licensing approaches will be acceptable to corporations?

Gilead

- Sell at cost of production and distribution in sub-Saharan Africa
  - $17.50 per month
- Has licensed 9 Indian generic manufacturers
  - Pay Gilead a 5% royalty
  - Make a profit
  - $8.75/month

Boston University

- Adopted global health licensing principles in October 2007
  - Process underway to make it a University policy
- Non-assert approach
  - Limited to public sector programs
- Sixlicenses completed to date
  - Five faculty start-ups
  - One publicly traded diagnostic company
  - One preferred an alternative approach to non-assert
  - First one approaching a big pharma partnership
- Including global health protections in:
  - Therapeutics and prophylactics
  - Diagnostics
- Not including in:
  - Tools
  - Devices

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AUTM Announces Global Health Initiative

AUTM announced the launch of a new Global Health Initiative that promotes licensing practices that support access to essential medicines by developing countries. The initiative includes a Global Health Toolkit created by AUTM members.

In keeping with this initiative, AUTM endorsed the *University Principles on Global Access to Medicines.* These principles were developed by a team that included AUTM leadership. Read the press release about the AUTM Global Health Initiative and AUTM's endorsement of the Principles.

Your institution can endorse the Principles here.

Read the Nine Points to Consider in Licensing University Technology

Endorse the Nine Points to Consider

Network with AUTM

Follow us on

Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies

Background

Universities have a fundamental role in fostering public health. Their greatest contributions may occur through discovery of new knowledge, education of students, and dissemination of knowledge for others to build upon through publications, library collections, and most recently, open courseware.

In addition, universities in the developed world work to facilitate the commercialization of the health-related inventions of academic researchers by developing and disseminating these technologies for the public good. We have created new methods to deploy cutting-edge knowledge toward potential public benefit by enticing risk takers to invest in our early stage technology in the hope of possible downstream commercial applications. In recent years, the licensing practices involved in such commercialization have expanded to promote explicitly global access to university-developed technologies, ensuring that advances in health reach those who need them most.

This sensitivity to global health was reflected in *Nine Points to Consider in Licensing University Technology,* a statement endorsed by nearly seventy universities and other organizations since the spring of 2007. In acknowledgement that conventions in this field are ever evolving, and building on recent experience, the institutions named below believe a more concrete statement of goals as well as licensing practices would help to promote further progress in advancing health in developing countries. The principles

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Click here to download the Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies (PDF file)

Click here to endorse the Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies on behalf of your institution.

The AUTM Global Health Toolkit includes AUTM position documents, relevant papers and articles on global health issues and sample licensing clauses.

Current Signatories:

Institution	Signing Date
Association of University Technology Managers	11/09/2009
Boston Univ	11/09/2009
Brown Univ	11/09/2009
Harvard Univ	11/09/2009
Univ of Pennsylvania	11/09/2009
Yale Univ	11/09/2009
Oregon Health & Science University	11/09/2009
National Institutes of Health	11/10/2009
University of Illinois Chicago	11/10/2009
University of Illinois Urbana-Champaign	11/11/2009
Centers for Disease Control and Prevention	11/12/2009
University of Vermont and State Agricultural College	11/19/2009
Duke University and Duke Medicine	12/01/2009
University of British Columbia	01/10/2010
Bilkent University	01/27/2010
El Colegio de México	01/27/2010
New York University	02/04/2010
Tecnologico de Monterrey	02/13/2010
Jawaharlal Nehru University	02/18/2010
Najit Technologies, Inc.	03/04/2010
Brigham & Women's Hospital	03/15/2010
Florida State University	03/29/2010
Massachusetts General Hospital	03/29/2010

Questions?

astevens@bu.edu