Innovation to Commercialization: Our Role Models

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I’ll either find a way... or make one

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Quest to Improve Human Health

Early stage Drug Discovery engine in place...
"Don’t worry. All you need is a revolutionary miracle drug that will be the medical discovery of the century. I'll see what I can whip up."
Getting pharmaceutical R&D back on target

Mark E Bunnage

The pharmaceutical industry is in a period of crisis due to the low number of new drug approvals relative to the high levels of R&D investment. It is argued here that improving the quality of target selection is the single most important factor to transform industry productivity and bring innovative new medicines to patients.

Nature Chemical Biology, vol 7, June 2011, 335-339
Figure 1 | Large pharma productivity from 2005–2010. Combined FDA-approved NMEs versus R&D spending for nine large pharmaceutical companies (AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Merck, Novartis, Pfizer, Roche and Sanofi-Aventis). Figures shown are in millions of US dollars. Source: FDA CDER; Bernstein¹. NME includes biologicals and vaccines.
Founded in 1935, Cipla makes drugs to treat cardiovascular disease, arthritis, diabetes, weight control, depression and many other health conditions, and its products are distributed in more than 180 countries worldwide.

Cipla is best-known outside its home country for manufacturing low-cost anti-AIDS drugs for HIV-positive patients in developing countries.

Founded by nationalist Indian scientist Khwaja Abdul Hamied.
Cipla Ltd. – A Brief History

Khwaja Abdul Hamied, the founder of Cipla, (born on October 31, 1898).

Mahatma Gandhi Visit to Cipla, July 4, 1939
Cipla is the world's largest manufacturer of antiretroviral drug (ARVs) to fight HIV/AIDS as measured by units produced and distributed.

Roughly 40 percent of HIV/AIDS patients undergoing antiretroviral therapy worldwide take Cipla drugs.

Cipla reduced the cost of providing antiretrovirals to AIDS patients from $12,000 and beyond (monopoly prices charged by international pharma conglomerates) down to under $100 per year.
Dr. Kiran Mazumdar Shaw, Biocon

Born on March 23, 1953 in Bangalore, India Mazumdar-Shaw completed her schooling from the city’s Bishop Cotton Girl’s High School (1968). She did BSc Zoology Honours course from Mount Carmel College, Bangalore University (1973). She later did her post-graduation in Malting and Brewing from Ballarat College, Melbourne University (1975).

She worked as a trainee brewer in Carlton and United Breweries, Melbourne and as a trainee maltster at Barrett Brothers and Burston, Australia.

Net worth
US$900 million (2010)
In 1989, Biocon became the first Indian biotech company to receive US funding for proprietary technologies. In 1990, she upgraded Biocon’s in-house research program, based on a proprietary solid substrate fermentation technology.

In 2007-08, a leading US trade publication, Med Ad News, ranked Biocon as the 20th leading biotechnology companies in the world and the 7th largest biotech employer in the world. Biocon also received the 2009 BioSingapore Asia Pacific Biotechnology Award for Best Listed Company.

Biocon is building cutting-edge capabilities, global credibility and global scale in its manufacturing and marketing activities. It has Asia’s largest insulin and statin facilities as also the largest perfusion-based antibody production facilities.
She started Biocon in 1978 and spearheaded its evolution from an industrial enzymes manufacturing company to a fully integrated bio-pharmaceutical company with a well-balanced business portfolio of products and a research focus on diabetes, oncology and auto-immune diseases.

She also established two subsidiaries: Syngene (1994) to provide development support services for discovery research and Clinigene (2000) to cater to clinical development services.

She was recently named among TIME magazine’s 100 most influential people in the world.

She is on the Forbes list of the world’s 100 most powerful women and the Financial Times’ top 50 women in business list.
Philanthropic Activities

Biocon Foundation (2004-) to conduct health, education, sanitation, and environmental programs to benefit of the economically weaker sections of society.

The Biocon Foundation's 7 ARY clinics are located where healthcare facilities are poor and they offer clinical care, generic medicines and basic tests for those who cannot afford them.

Each of the clinics serves a population of 50,000 people living within a radius of 10 km. Each year, the Foundation touches more than 300,000 lives through its holistic healthcare approach.

Established a 1,400-bed cancer care center at the Narayana Health City campus at Boommasandra, Bangalore, along with Dr. Devi Shetty of Narayana Hrudayalaya in 2007.
Dr. Reddy's Laboratories Ltd. is an integrated pharmaceutical company focused on providing medicines through its three business segments: Global Generics segment, Pharmaceutical Services and Active Ingredients (PSAI) segment and Proprietary Products segment.

The company was founded by Dr. Anji Reddy, who had previously worked in the publicly owned Indian Drugs and Pharmaceuticals Limited of Hyderabad, India.

Dr. Reddy's manufactures and markets a wide range of pharmaceuticals in India and overseas.

The company has over 190 medications, 60 active pharmaceutical ingredients (APIs) for drug manufacture, diagnostic kits, critical care, and biotechnology products.
Early Life and Education

Dr. Reddy spent his early years in the village of near suryapet nalgonda in nalgonda District, where his father grew turmeric.

He studied in Anapothana ZPHS School in Nutakki until Tenth Class.

Dr. Reddy after graduating from the local high school, went on to get his first Bachelor of science degree from A.C. College at Guntur in 1958.

Thereafter he, did his B.Sc.-Tech in Pharmaceuticals and Fine chemicals from Bombay University followed by a Ph.D. in chemical engineering from the National Chemical Laboratory, Pune in 1969.

Started Dr Reddy's Labs in 1984 with an initial capital of Rs 25 lakh (Rs 2.5 million).

Over the years, it transformed Indian bulk drug industry from import-dependent in mid-80s to self-reliant in mid-90s and finally into the export-oriented industry.
Investment in R&D

Dr. Reddy's Research Foundation was established in 1992 and dedicated to research in area of new drug discovery.

In 2000, the Foundation set up an American lab in Atlanta, dedicated to discovery and design of novel therapeutics.

The lab is called Reddy US Therapeutics Inc (RUSTI) and its main aim is the discovery of next-generation drugs using genomics and proteomics.

Reddy's research thrust focused on large niche areas in western markets – anti-cancer, anti-diabetes, cardiovascular and anti-infection drugs.
Philanthropic Activities

*Naandi Foundation*, a not-for-profit development institution that strives for eradication of poverty has Dr Reddy as its founding father. He is also founder-chairman of Dr Reddy’s Foundation for Human and Social Development, a social arm of Dr. Reddy’s Labs.
Recognized institutional builder and respected scientist with over 35 years experience in research and leadership. Former director of the Indian Institute of Chemical Technology (IICT) - managing over 1,400 employees including 500 scientists
Born on the 2nd of April, 1935 in the city of Guntur, Andhra Pradesh, India.

Degree in chemistry in 1956 from Andhra University and postgraduate degree in Chemical Technology from Bombay University in 1960.

Obtained his Ph.D. (Tech.) under the supervision of Prof. Venkataraman, the first Indian Director of National Chemical Laboratory, Pune.
Post-doctoral Studies with Prof. E. J. Corey (1991 Nobel Laureate) at Harvard University.

After spending two years in E.J Corey’s group (1975-'77), he returned to NCL and established a school of excellence for the synthesis of bio-functional molecules in India.

What Corey has to say About Dr. Rama Rao:

“your superb role as a leader of chemical synthesis in India is well-known and much admired”
Dr. Rama Rao’s contribution to chemistry and medicine emerges from his studies on natural products and organic synthesis, and is spread over 250 research papers and several patents.

Trained 109 graduate students for their Ph.D degrees and several post-doctoral fellows.

He is responsible for initiating process chemistry in India and giving a fillip to the Indian Pharma industry in producing several life saving drugs at affordable prices.
Dr. Rama Rao initiated work on AZT (Azidothymidine), the first curative agent for AIDS, and came out with an innovative and cost-effective approach that was used by CIPLA in introducing the drug in India at a cost of $0.30 per capsule against the international price of $3.0.
Dr. S. K. Joshi, Former Director General, CSIR, states,

“Today the drug industry has a firm base of indigenous production and has made a mark in export markets; much of credit directly or indirectly goes to Dr. Rama Rao.

He is the man with the ‘Midas touch’ who transforms any drug process development project to a roaring commercial success.”
Dr. Rama Rao has proved to be an outstanding scientific administrator too. Under his leadership (1985-1995) IICT emerged as CSIR’s most reputed institution in chemical sciences and technology.

Sir John Madox, Editor, “Nature” (Nature 366,626, Dec. 16th 1993) wrote thus: “the most improved laboratory in India must be the Indian Institute of Chemical Technology at Hyderabad. The difference is not so much the change of name, but the arrival as Director of Dr. Rama Rao, a vigorous no-nonsense organic chemist of distinction.”
Dr. Rama Rao spurred on by his unending zest for research in science and technology and his keenness to cater to the needs of pharmaceutical companies, went on to utilize these facilities fruitfully and established **AVRA Laboratories**.
Dr. Rama Rao is probably the most outstanding ‘technopreneur’ India has produced in the post-independent era with the unusual combination of world class academic excellence, skills in developing globally competitive technologies and entrepreneurship in setting up a flourishing knowledge-based industry.
Programmed Cell Death

Normal Tissue
- New Cells
- Cell Death
- Homeostasis

Diseases of Disordered Cell Death
- New Cells
- Cell Death
- Neurodegeneration
- Immunodeficiency
- Infertility
- Cancer
- Autoimmunity
Academic Research to Commercialization

HUMAN GENOME SCIENCES AND AEGERA THERAPEUTICS ANNOUNCE LICENSING AND COLLABORATION AGREEMENT ON NOVEL ANTI-CANCER DRUGS

- HGS acquires exclusive rights to develop and commercialize small-molecule IAP inhibitors in oncology -

- Lead compound AEG40826 works synergistically with HGS TRAIL receptor antibodies to enhance anticancer activity of both drugs -

- IAP inhibitors also show promise alone and in combination with other anti-cancer agents across broad range of cancers -
ROCKVILLE, Maryland and MONTREAL, Quebec – December 20, 2007 – Human Genome Sciences, Inc. (Nasdaq: HGSI) and Aegera Therapeutics Inc. today announced an agreement under which HGS has acquired exclusive worldwide rights (excluding Japan) to develop and commercialize AEG40826 and related backup compounds to be chosen during a three-year research collaboration. AEG40826 is a potent small-molecule inhibitor of multiple IAP (inhibitor of apoptosis) protein family members that is expected to begin oncology clinical trials in early 2008.
Under the agreement, HGS has paid Aegea an upfront license fee of $15 million and has made an equity investment of C$5 million. Aegea will be entitled to receive up to $295 million in future development and commercial milestone payments, including a $5 million milestone payment upon FDA clearance of an IND. Aegea will receive double-digit royalties on net sales in the HGS territory. In North America, Aegea will have the option to co-promote, under which it will share certain expenses and profits (30%) in lieu of its royalties. Aegea retains the non-oncology rights to its IAP inhibitors that are not selected for development under this agreement.
Regulation of oncogene-induced apoptosis

PhD (1974), McGill University
Hunt for Highly Selective Anti-Cancer Drugs!
GeminX Pharmaceuticals specializes in the discovery and development of novel small-molecule cancer therapeutics based on the regulation of apoptosis, the body’s natural ability to destroy injured or damaged cells.

GeminX’s lead product, GX15-070, is a small-molecule, pan-inhibitor of Bcl-2 proteins.

GeminX is also developing small molecules that induce apoptosis in p53-defective cancers.
Cephalon to Acquire Gemin X for $225M (March 2011)

Cephalon Inc. said on Monday it will acquire privately held Gemin X Pharmaceuticals Inc. for $225 million in an all-cash deal aimed at bolstering Cephalon's lineup of cancer treatments.

Cephalon said Gemin X's private shareholders could receive as much as an additional $300 million in cash payments if certain regulatory and sales goals are met.

Cephalon would have no royalty obligations to Gemin X shareholders under the transaction, which is subject to regulatory clearances and other conditions. After the deal's expected closure in this year's second quarter, Gemin X would become a wholly owned subsidiary of Cephalon.
**Taxol Natural Product as Anti Cancer Drug**

**Paclitaxel** is a mitotic inhibitor used in cancer chemotherapy. It was discovered in a U.S. National Cancer Institute program at the Research Triangle Institute in 1967 when Monroe E. Wall and Mansukh C. Wani isolated it from the bark of the Pacific yew tree, *Taxus brevifolia* and named it **taxol**. When it was developed commercially by Bristol-Myers Squibb (BMS) the generic name was changed to **paclitaxel** and the BMS compound is sold under the trademark **TAXOL**.
MICROTUBULES AS A TARGET FOR ANTICANCER DRUGS

Mary Ann Jordan and Leslie Wilson

Highly dynamic mitotic-spindle microtubules are among the most successful targets for anticancer therapy. Microtubule-targeted drugs, including paclitaxel and *Vinca* alkaloids, were previously considered to work primarily by increasing or decreasing the cellular microtubule mass. Although these effects might have a role in their chemotherapeutic actions, we now know that at lower concentrations, microtubule-targeted drugs can suppress microtubule dynamics without changing microtubule mass; this action leads to mitotic block and apoptosis. In addition to the expanding array of chemically diverse antimitotic agents, some microtubule-targeted drugs can act as vascular-targeting agents, rapidly depolymerizing microtubules of newly formed vasculature to shut down the blood supply to tumours.

*Nature Reviews Cancer, Vol 4, April 2004, 253-265*
Botanist Arthur Barclay in hat, records a plant collection in the field, early 1960s.

...by Christmas of 1966 Wall was calling for 375 pounds of bark....for every 30 pounds he got, he was producing barely half a gram of K172.

World Beaters: A happy team of FSU Taxol researchers led by Bob Holton claimed victory in totally synthesizing the drug on Dec. 9, 1993.
Hope in a Bottle: Bristol-Myers Squibb introduced Taxol to the market place in January 1993. From bark to business, the process took 31 years.
Complex synthesis yields breast-cancer therapy

Drug approval marks culmination of a marathon trek from sea sponges to clinic.

Professor Y Kishi, Chem and Chem Biol, Harvard University

Halichondrin B

The drug eribulin (inset) was inspired by a compound from the sea sponge *Halichondria okadai*.

*Nature, 468, Dec 2 Issue 2010, 609-610*
EISAI ANNOUNCES COMMENCEMENT OF OPERATIONS OF A NEW RESEARCH FACILITY AT H3 BIOMEDICINE INC., A U.S. RESEARCH SUBSIDIARY TO FACILITATE CUTTING-EDGE CANCER GENOMICS-DRIVEN DRUG DEVELOPMENT

-Aims to Provide Personalized Medicine by Integrating Next-generation Synthetic Organic Chemistry with Patient-Based Cancer Genetics-

Pictured from left to right: Dr. Stuart Schreiber, Mr. Haruo Naito, Dr. Markus Warmuth and Dr. Todd Golub
Human Genome Project
New Research Models

NIH Dives Into Drug Discovery

NIH unveils an ambitious plan to create molecular libraries as a first step to finding potential new drugs. But is it feasible?

McGill Life Sciences Complex

Ontario Inst of Cancer Res
Toronto

Burnham Institute
Role Models to Follow

UK-CANADIAN CONSORTIUM COMMITS $95 MILLION TO THE LARGEST INTERNATIONAL HEALTH RESEARCH PROJECT EVER FUNDED IN CANADA

April 3, 2003 Announcement of Canadian funding of the International Structural Genomics Consortium at the Vivian and David Campbell Conference Facility in the Munk Centre for International Studies at the University of Toronto. From left to right: Member of Parliament Tony Ianno, Dr. Cheryl Arrowsmith, scientific director for the SGC Canadian research team, Associate Minister for Enterprise, Opportunity and Innovation David Turnbull; Prof. Aled Edwards, chief executive officer of the SGC, Ontario Premier Ernie Eves, Industry Minister Allan Rock, U of T President Robert Birgeneau.
Role Models to Follow

Philanthropists Eli & Edythe Broad of Los Angeles Give $100M to Create Institute with MIT, Harvard, and Whitehead To Fulfill Genome’s Promise for Medicine

Human Genome Leader Eric Lander to Head New Research Institute

Thursday, June 19, 2003

The Broad Institute’s mission will have two parts:

• To create comprehensive tools for genomic medicine and make them broadly available to scientists around the world.

• To pioneer applications of these tools to the study of disease, in order to propel the understanding, diagnosis, prevention, and treatment of disease.
Support of the Broad Institute

Eli and Edythe L. Broad: $100M (over ten years)
(doubled in a short duration)

Sept 2008, Declared this Institute Model a Success
Eli and Edythe L. Broad: $400M

The Stanley Medical Research Institute: The Stanley Center for Psychiatric Research was created in 2007
Support: $100M over ten years
Chemical Biology Program @ the Broad Institute

Schreiber Group Open House

Think different.

October 6, 1999    Graduate Student Lounge    5 pm

SCHREIBER OPEN HOUSE
Friday December 2, Fairchild Conference Room, 6:30 pm

NEED WE SAY MORE?

Schreiber Group Open House:
Tuesday, October 3rd, 6-9PM

Diversity-oriented synthesis and human health
The Broad Institute of Harvard & MIT
7 Cambridge Center, Kendall Square
Shuttle from 7 Divinity Ave. departs @ 6:00PM

Small molecules synthesized or discovered by chemical biologists at the Broad Institute of Harvard & MIT’s Chemical Biology Program

BROAD INSTITUTE of HARVARD & MIT

1st year graduate students in CCB are invited to attend an Open House introducing the Broad Institute, the Schreiber group and the theme:

"Rethinking drug discovery using chemistry & chemical biology"

SCHREIBER LAB OPEN HOUSE: PRESENTATION, PORTER SESSION & FOOD

Tuesday, October 9th, 6 PM - Seven Cambridge Center
Kendall Station or Shuttle departs from @ 6:30PM
Stuart’s Contribution to Three Major Spin Outs

Monday, March 6, 2006

Pharma

Infinity-Novartis deal could top $400M

Infinity Pharmaceuticals Inc. reports it has entered into a global strategic alliance with Novartis to discover and commercialize drugs targeting Bcl-2 protein family members for the treatment of a broad range of cancers.

Under the terms of the agreement, Cambridge-based Infinity would receive $30 million in up-front license fees, an equity investment and committed research funding during the first two years of the relationship. Along with success-based milestones, total payments to Infinity could exceed $400 million. Upon commercialization, Infinity has an option to co-commercialize Bcl-2 family inhibitors in the United States.
Aim to Develop the Leaders of Tomorrow

Knowledge-based Economy