The Biotech Perspective on Reliable Manufacturing

Markus Gemuend
Vice President, Manufacturing Collaborations

Genentech, Inc.
South San Francisco, California

June 7th, 2005

Genentech – DNA by the Bay

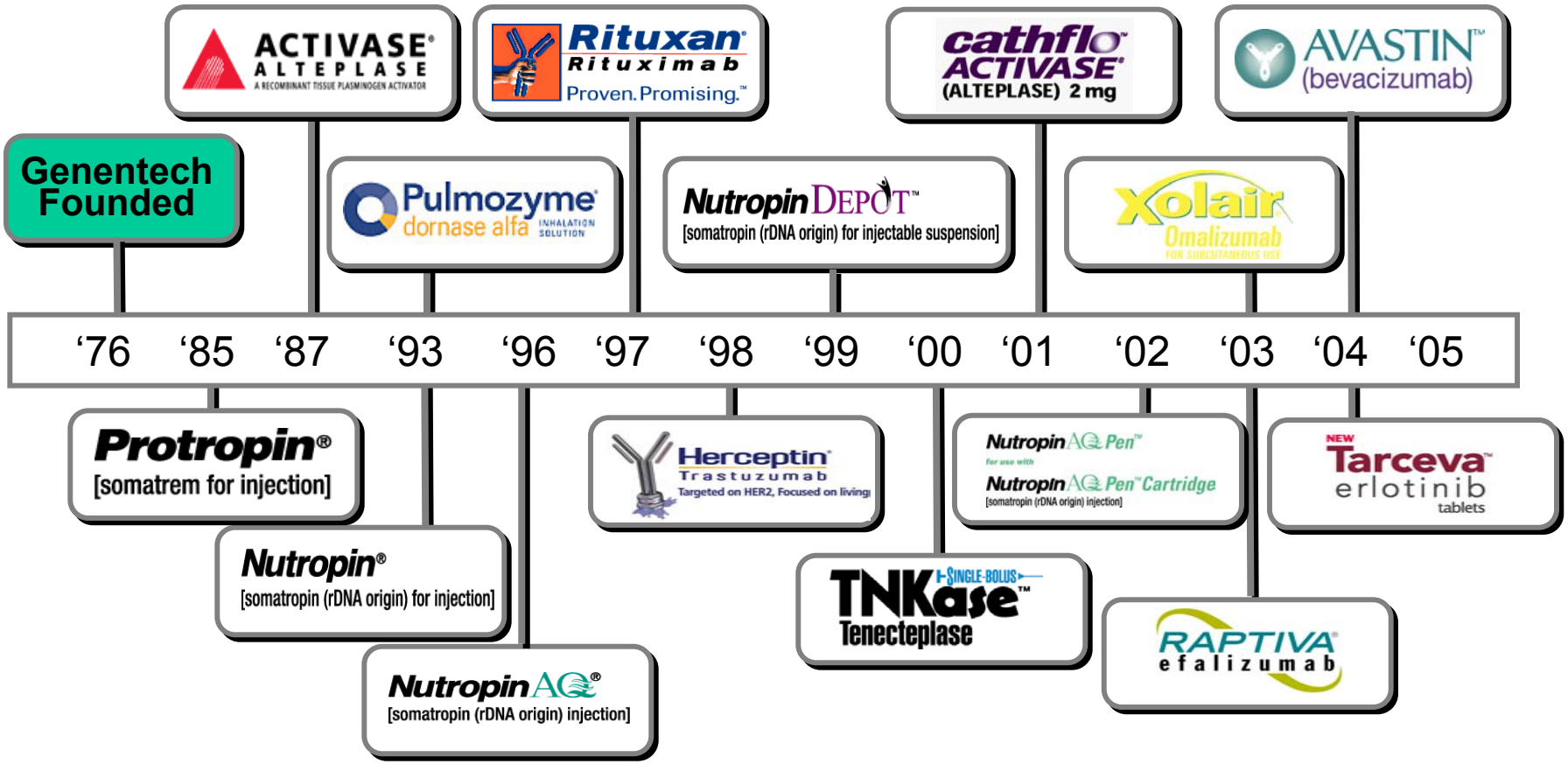
Our mission is to be the leading biotechnology company, using human genetic information to discover, develop, manufacture and commercialize biotherapeutics that address significant unmet medical needs.

We commit ourselves to high standards of integrity in contributing to the best interests of patients, the medical profession, our employees and our communities, and to seeking significant return to our stockholders based on the continual pursuit of ***scientific and operational excellence****.*

Genentech was the first biotechnology company and is a world leader in protein production

- Founded in 1976 by biochemist Herb Boyer and venture capitalist Bob Swanson
- Revenue was $4.6 billion in 2004
- Year-end 2004 we had 7,646 employees
- Three manufacturing locations (South San Francisco, Vacaville, and Spain)
- More than 30% of worldwide production of therapeutic proteins
- 12 marketed products - 37 SKUs
- Over 30 projects in development

Over 25 Years of Excellent Science



Protropin manufacturing was discontinued at the end of 2002. Nutropin Depot commercialization was discontinued in June 2004; we are working to transition our existing Nutropin Depot patients to another Nutropin product.

Employer of Choice

Science Magazine

- Named the “Top Employer and Most Admired Company in the Biotech and Pharma industries” for the second year in a row

Science 2003
TOP EMPLOYER

Fortune

- Named one of the “100 Best Companies to Work For” for the 7th consecutive year

Essence

- Listed as one of the 17 “Great Places to Work”

ESSENCE

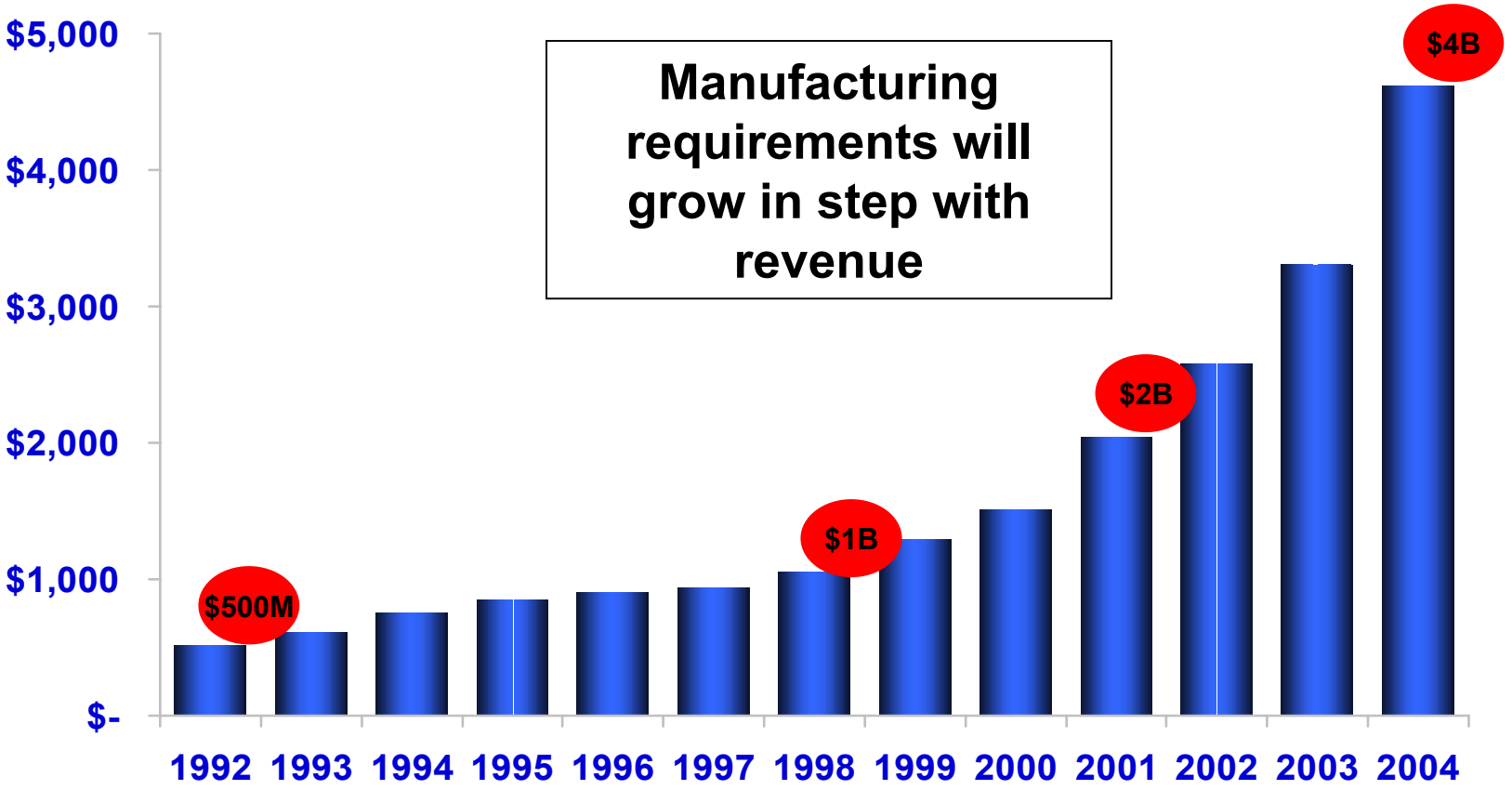
The Black Collegian

- Named to the “Top 100 Employers” list

THE BLACK COLLEGIAN Online
The Career Site for Students of Color

Our revenues have doubled in the last few years

TOTAL OPERATING REVENUES (USD$ IN MILLIONS)



The Reality

Research Excellence alone is no longer sufficient for success.

Manufacturing Excellence is a must – this is the ultimate consequence of customer power, technology and competition.

How are we planning to reliably deliver product to ensure the company's continued success?

- Capacity Planning
  - What has history taught us?
  - What affects our planning (and how is that different than Pharma)?
  - What do we consider?
- Operational Excellence
  - The mindset
  - The leadership
  - Defining "world-class"
  - Knowing our methodology

Capacity planning has been historically difficult

- Always have capacity – but not too much capacity!
  - Immunex
    - Insufficient capacity for Enbrel
  - IDEC
    - Insufficient cash and capacity to make Rituxan
  - Pharma
    - Excess capacity

How has Genentech historically planned capacity?

- We can build plants…
  - 1981: South San Francisco
  - 1998: Vacaville
  - Estimated 2009: Vacaville
- But process and technology improvements are necessary to lower cost of goods and ensure capacity for future products
  - Science is rapidly changing our processing capabilities
    - Cell expression is increasing multi-fold - faster than we build plants!
  - Product development timelines require us to build capacity for products before we know entirely what the manufacturing process will be

What are we doing now to plan capacity?

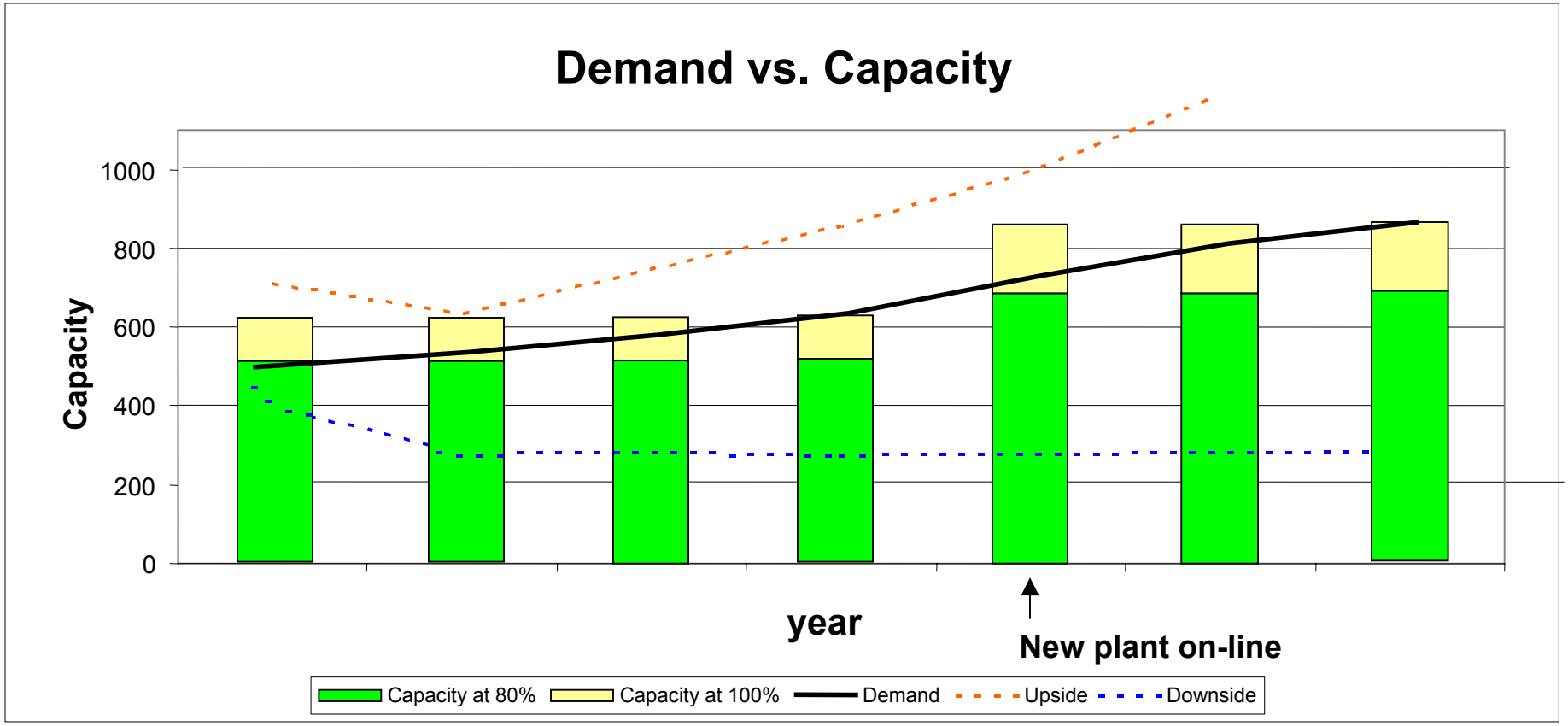
- Sales and Operations Planning Process (S&OP)
  - Decision making with a 3 year vision to ensure we match capacity to demand
- Strong process development to drive down costs and ensure capacity fit with our future pipeline
  - Improve yields / titer
  - Optimize utilization of manufacturing capacity
  - Increase process robustness and reliability

What challenges does Biotech face that differ from Pharma?

Differences in Biotech vs. Pharma Capacity Planning	
Protein Production	API
5-6 year lead time to build new facilities	shorter lead time to build new facility
Rate of technology change high	Technology not changing rapidly
Processes require fit with facility – modifications required to fit	Less complicated processes allow for easier plan changes
No robust CMO market	Excess capacity in industry

How much capacity is enough?

When would you want a new plant to come on line?



Capacity Management Strategies

- Reclaim Capacity From Your Existing Facilities
  - Improve Yield, Up Time, Run Rate, Success Rate
  - Reduce Cycle Time
  - Improve Reliability
- Buy Capacity
  - Contract Manufacturing (e.g., Lonza)
  - Collaborations
- Build Capacity
  - Forecast, Plan and Invest Early
  - Decrease time to build
    - Concurrent engineering and modular technology

In the long term, an efficient and effective cost structure is primarily a consequence of good capacity management strategies

Relentless pursuit of Operational Excellence is critical to our ability to deliver

- **Operational Excellence** is a **mindset:**
  - It's about **NEVER** being satisfied with **Average** performance.
  - It's a **Burning Desire** to drive waste out of the system.
  - It's knowing when to be **Innovative** and when to be **Disciplined.**
- ***But most of all, it's about …..***

Eight Manufacturing Leadership Attributes necessary for Operational Excellence

1. Passion for operations – Always connected with Reality. 24x7 availability when your organization needs you.
2. Ability to Facilitate, Energize, Teach and Lead
3. Ability to Hire, Develop and Build a great team
4. Principle centered - Predictable behavior
5. Relentless follow-up - Deliver results
6. Attention to Details - Nothing falls through the crack
7. Emotional Strength – Have the Edge to make tough decisions and the Heart to implement it thoughtfully
8. Emotional Intelligence – For interpersonal productivity, collaboration and team achievements

In our pursuit of Operational Excellence, we need to define What world-class operations look like

Customer Service	Deliver the right products, in the right quantities, on time, as planned.
Quality	Do it Right the First Time
Compliance	Always inspection ready that results in positive inspection outcomes and rapid regulatory approvals
Productivity	A cost structure that is competitive (top 20%) within the Pharma/Biotech Industry
EH&S	Unsafe behaviors are almost never seen and all known causes of unsafe situations/behaviors have been virtually eliminated by the work group (IRR rate in 95th percentile for industry).
Leadership	Drive a Culture of Operational Excellence as a way of life

To achieve business process excellence… it takes:

- Strong process owners
  - Executive-level individuals, with process authority
- Process metrics
  - The framework for stretch goals
- Dedicated process design teams
  - Working across boundaries
- Effective methodology
  - Discipline, teamwork and alignment
- Passionate executive leadership
  - Insistence on results and the willingness to do whatever is necessary
- Strong Governance
  - Oversight at the very top
- Line Management Accountability
  - Ownership and engagement at all levels

Our Operational Excellence Methodology is not just tools – it is management of those tools to achieve optimal results

The Methodology is……

- A Six Sigma based tool for process improvement
- A broad array of tools and templates available for use where appropriate
- An opportunity to establish consistency in process and language for all efforts
- A Framework for solving problems and sustaining results

The Methodology is <u>not</u>…

- A substitute for good management
- A substitute for common sense
- A rigid checklist
- A pure science

Why is manufacturing reliability so vital?

"No patient will go without…"


Carol, Rituxan patient


Marilyn, Herceptin patient