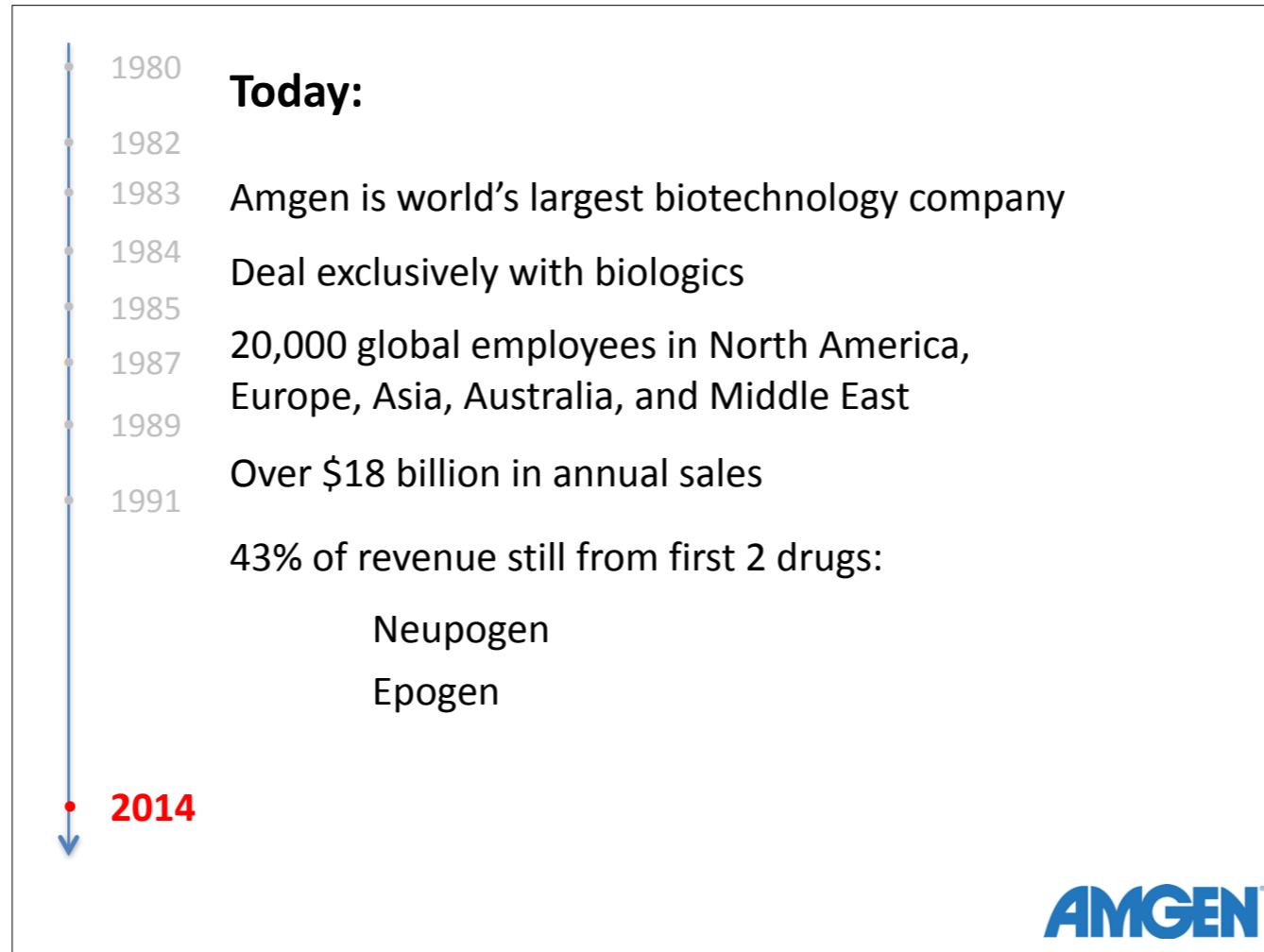




Case Study:

From humble beginnings to world's
largest biotech

September 29, 2104



Biologics: medicinal products manufactured or extracted from biological sources-used extensively for producing regenerative medicines

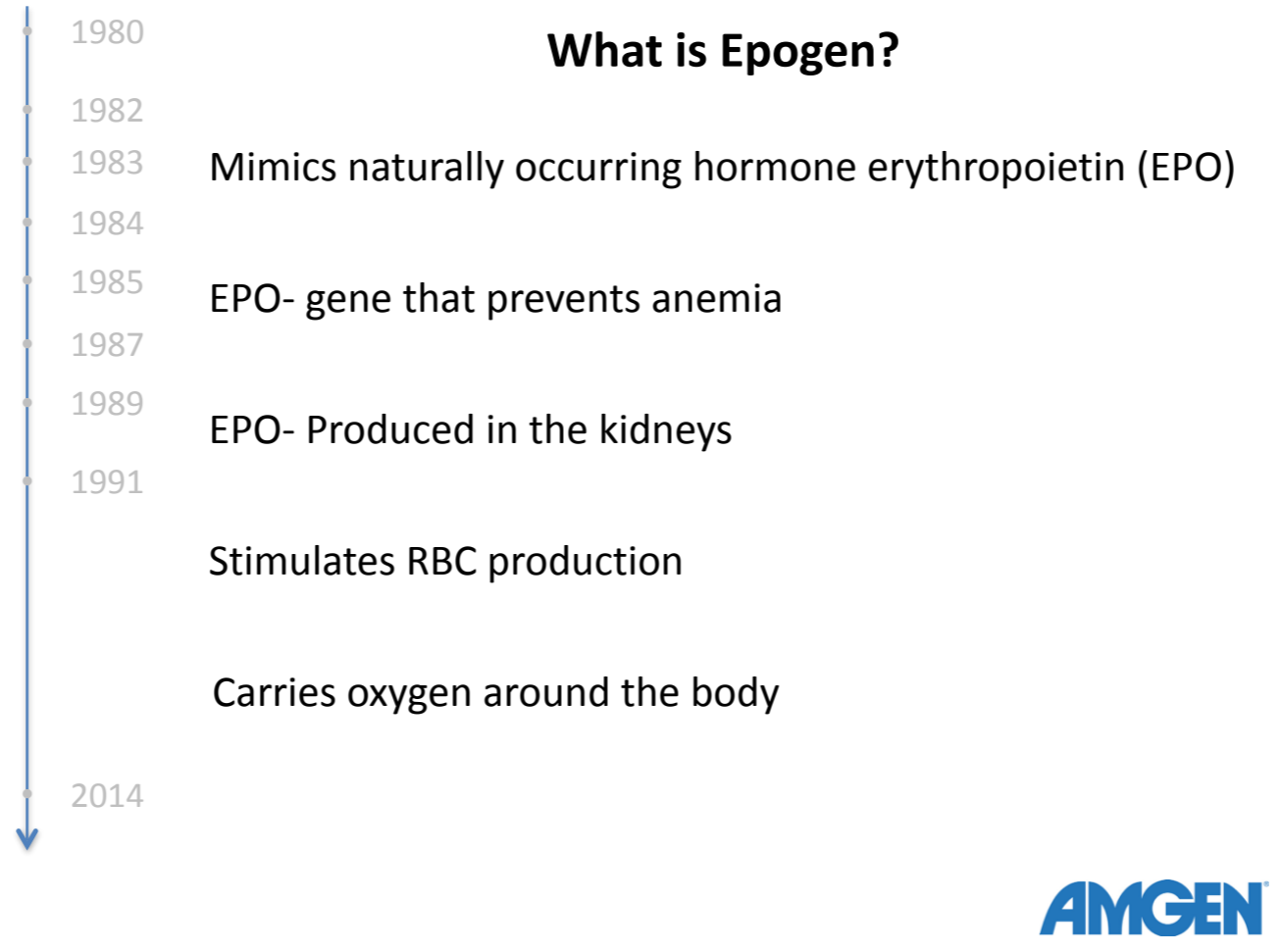
This is the story of the development of Epogen

World's first biotech blockbuster drug

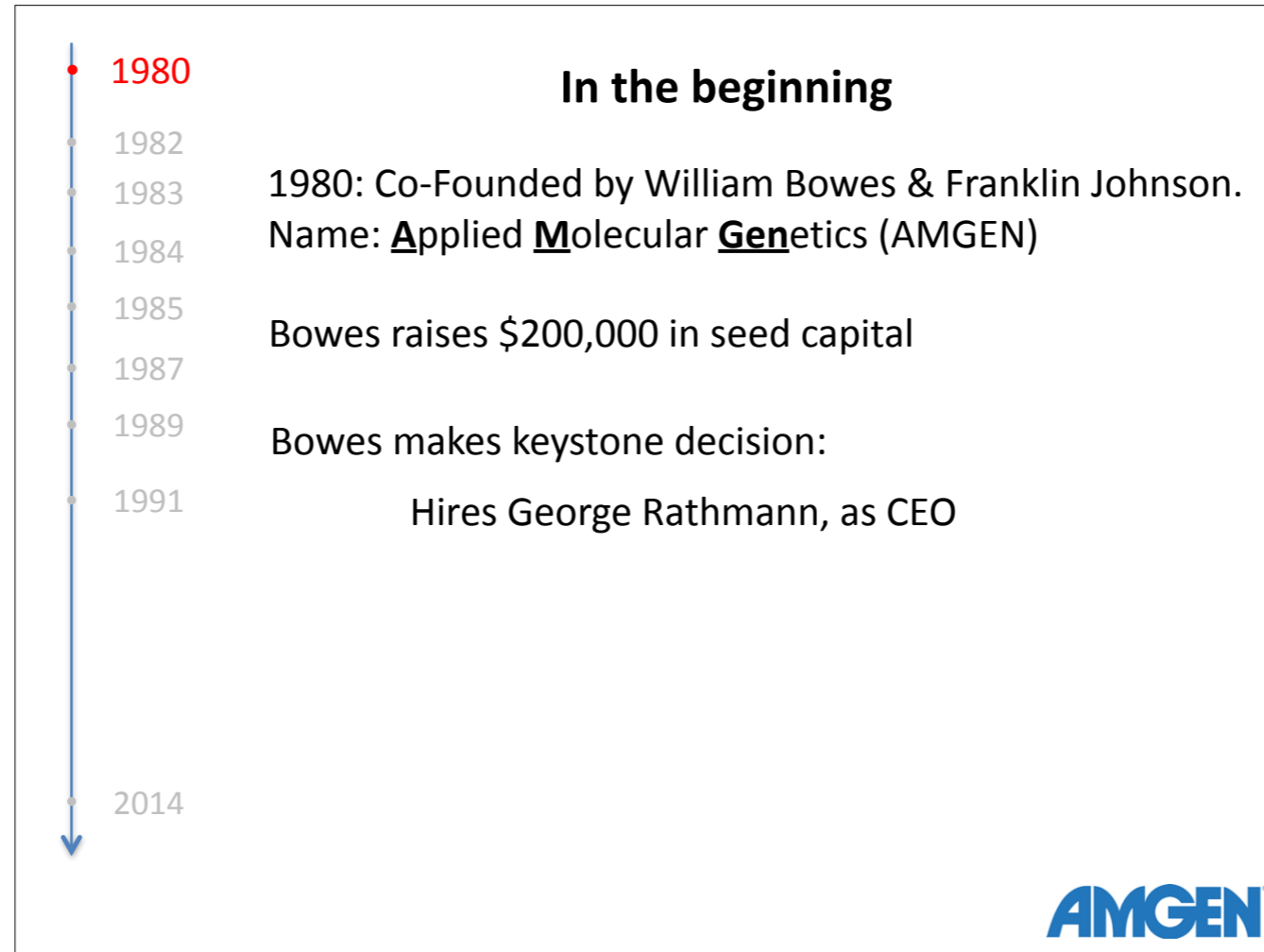
Made Amgen who they are today



What is Epogen?



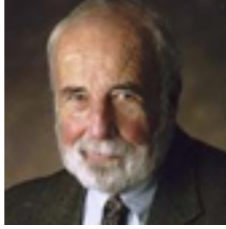
EPO is a gene that prevents anemia. Anemia can affect people with Chronic Kidney Disease, but also therapy for patients receiving chemotherapy treatment. Anemia leads to severe fatigue and increased risk of cardiovascular disease and even death.



1980: William Bowes left the world's first biotech company, Cetus Corp which was struggling in part due to bad management to co-found along with Franklin Johnson Applied Molecular Genetics. Now known as Amgen. Name change at 1983 IPO
Bowes raised \$200,000 in seed capital and made arguably the company's best decision in its 30 year history to hire George Rathmann to be CEO.

1980

George Rathmann




Prev. Dir Research Abbott Labs
20 years at 3M: Scotchguard and other products

Rare combination:

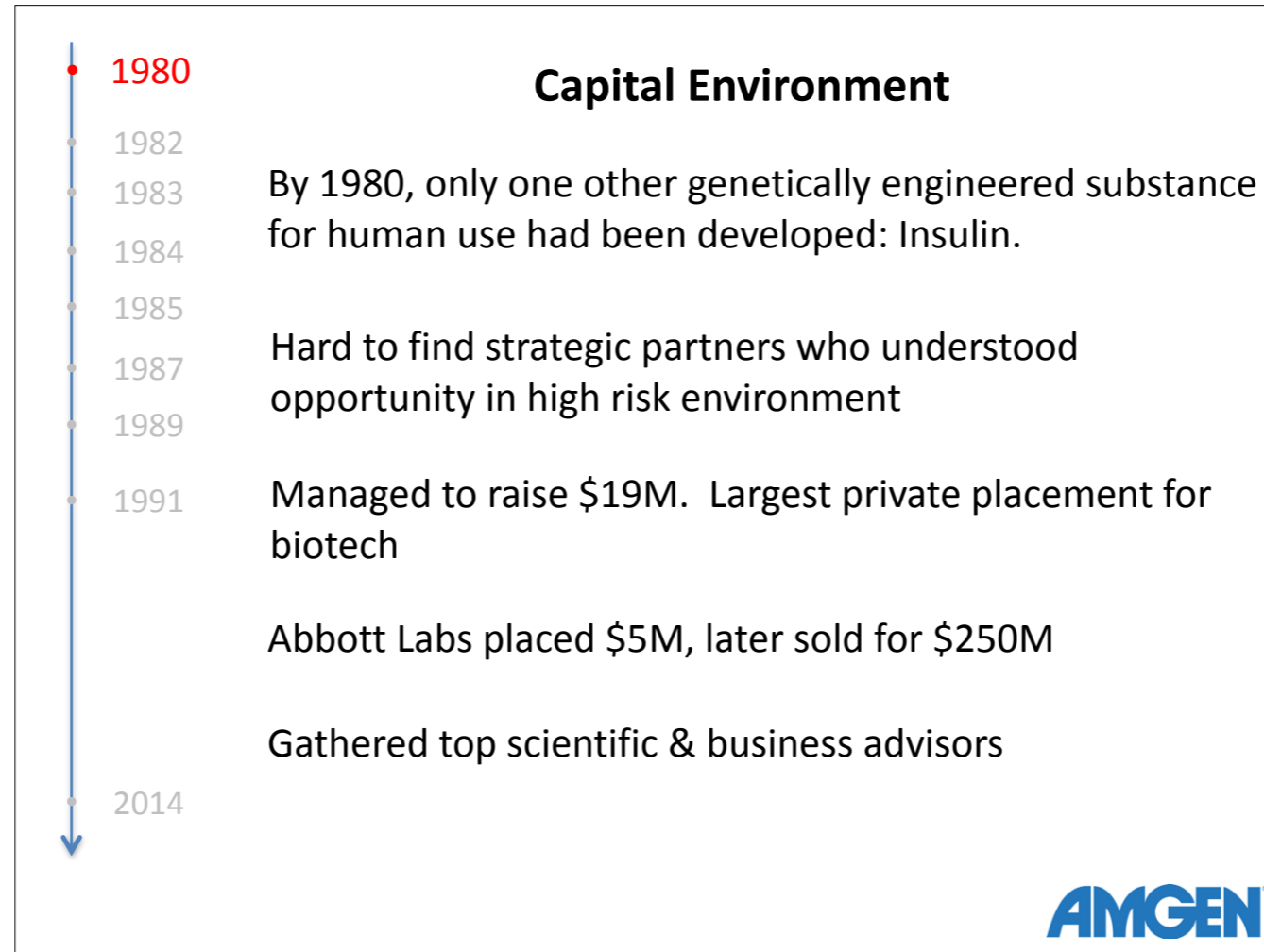
- Scientific Background
- Business Acumen
- Charisma

Widely considered one of fathers of biotech industry

2014



Ironically Rathmann later died in 2012 from Kidney Failure, and had received Epogen treatment.



Aggressive financing round- looking for large investment.

19M in investments from large corporations, Abbott Laboratories and Tosco Corporation as well as VCs.



Genetech had just had a wildly successful IPO, Amgen was able to cash in on the temporary biotech craze on wall street.

Funds used to recruit top researchers from leading pharma cos

Ability to raise so much \$ saved company in impending FDA approval process and future legal battles

With \$- able to start identifying & developing products

Getting down to business



1983:

Grown to 185 employees

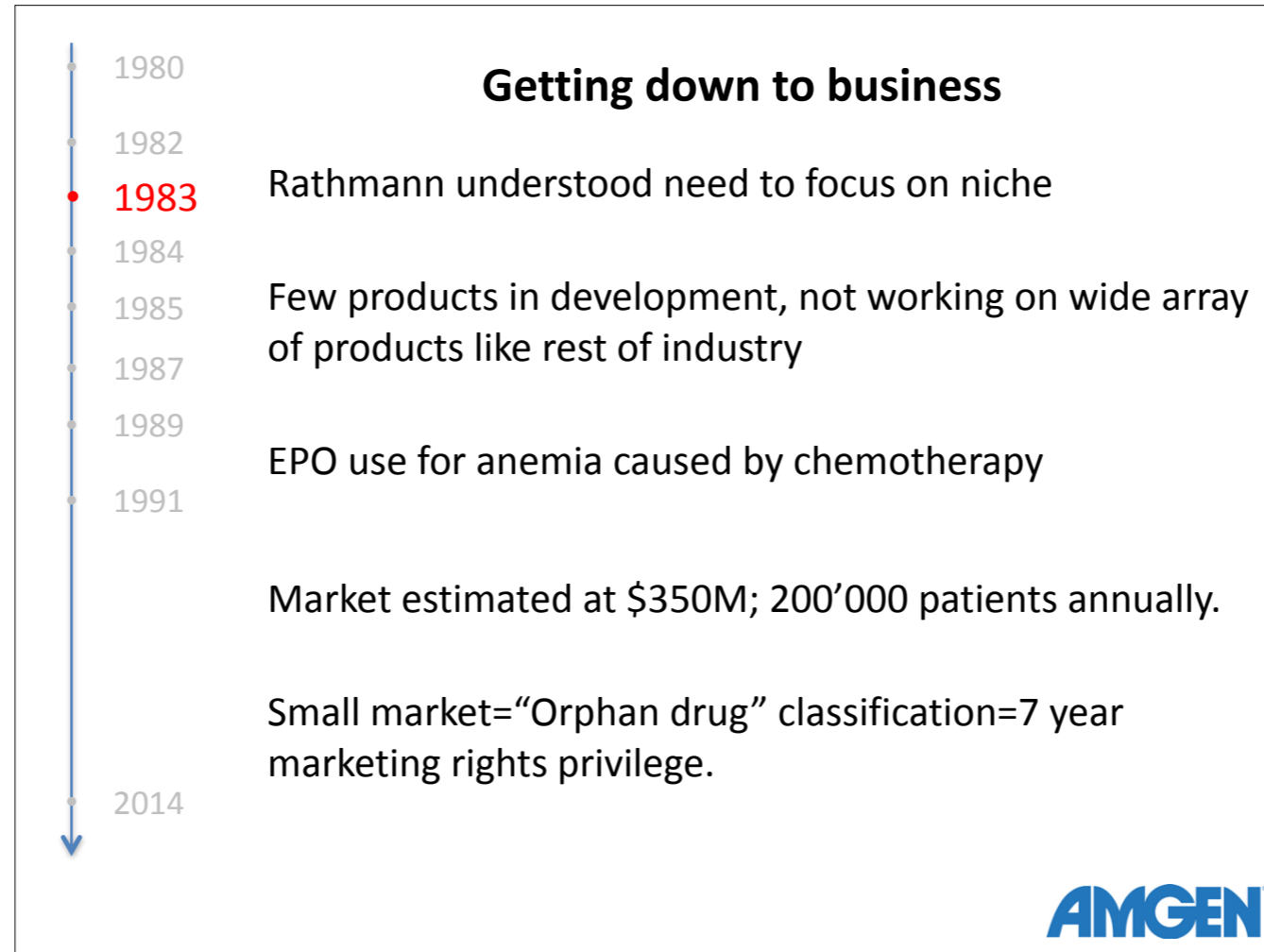
Lab space tight

Huge burn rate

No product yet for human market

Growth hormones for livestock to cover cash flow





Early on, Rathmann understood the need to focus on a niche product, so he and scientific team decided to focus on producing human erythropoietin (EPO). EPO would have uses for patients with Chronic Renal Failure as well as use prior to surgeries that would involve heavy blood loss and also for treating anemia that can be caused by Chemotherapy.

Success!



Amgen Scientist Fu-Kuen Lin isolates EPO gene
on one of 1.5 million fragments on DNA



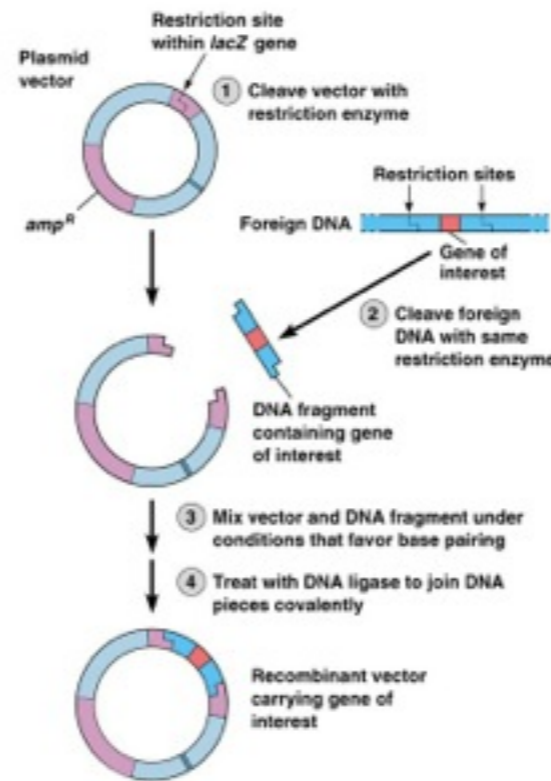
1980
1982
1983
1984
1985
1987
1989
1991

2014

Successfully transformed Chinese Hamster Ovary cells to produce biologically active EPO

Source: Addison Wesley Longman, Inc.

Success!



(b) Preparation of recombinant plasmid vector

© Addison Wesley Longman, Inc.



The host cell and its vector- genetically engineered cell

FDA & Patents



FDA application process initiated

Patents filed



Strategic Partnership



Success (?!)



1987: US PTO Responds to patent applications

Some patents approved, others not

1987

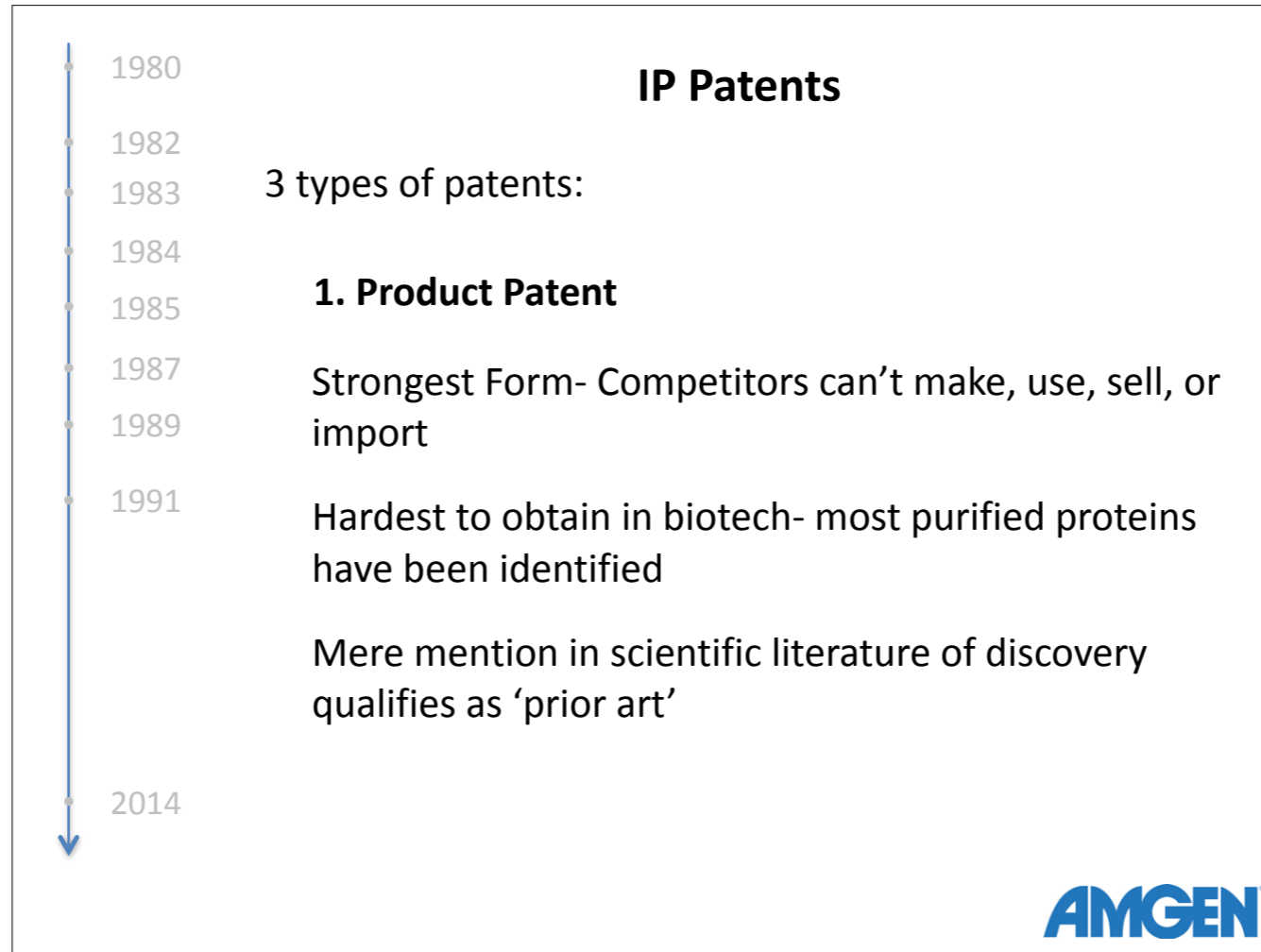


Patent Approval

3 Requirements:

1. Novel- first to make product
2. Nonobvious- no mention in prior art
3. Utility- Must be useful





Product patent. The strongest patent form. Covers the product. Competitors can't make, use, sell or import the product. Hardest to obtain in biotech, because many purified proteins have already been identified. The mere mention in scientific literature of discovery or isolation qualifies as 'prior art'. Example, Insulin, innovator Frederick Sanger succeeded in identifying the chemical structure in 1951 and went on to win the Nobel Prize, but couldn't win the patent because in 1921 physicians at Uni of Toronto had already isolated a small amount insulin.

IP Patents

3 types of patents:

2. Process Patent

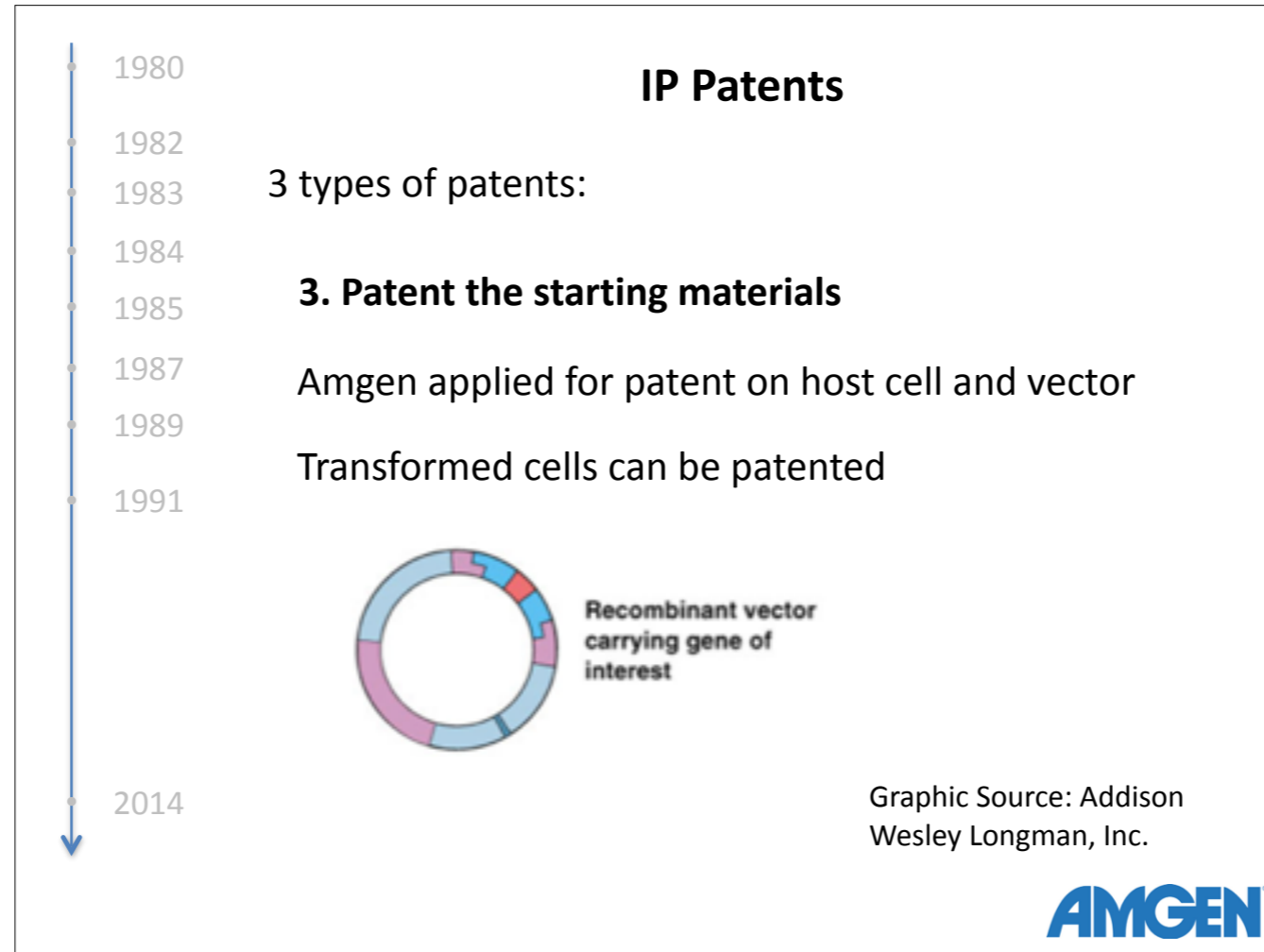
Covers the method of making product

Next best protection

To enforce- must prove competitor is using patented process

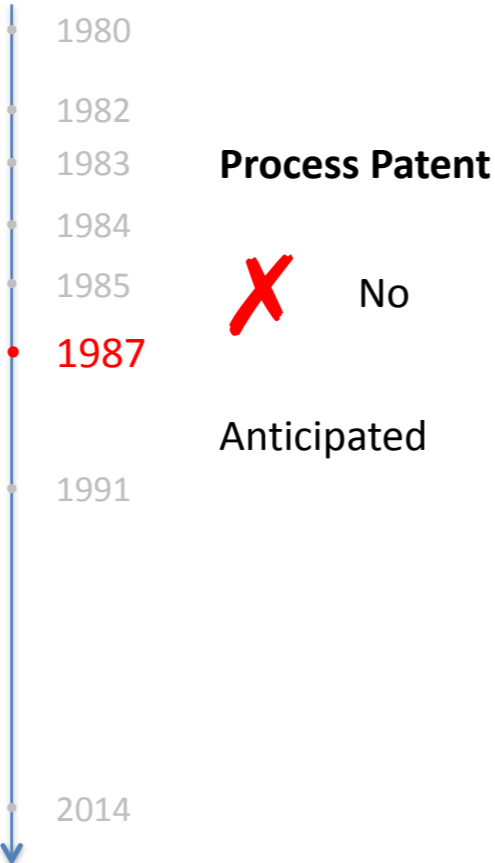
Hard to get since much of genetic engineering is based on similar methods for manufacturing human proteins





Patent the starting materials. In Amgen's case, they applied for a patent on the host cell and its vector. Once the vector was successfully incorporated the isolated gene into the host cell, the cell is said to be 'transformed.' Transformed cells could be patented as a type of 'machine' to further produce the desired proteins. The weakness with patents for starting materials is that they don't prevent foreign manufacturers from using starting materials and exporting the final drug to the United States.

IP Patents



IP Patents



Starting Materials Patent

✓ Yes

Anticipated



IP Patents



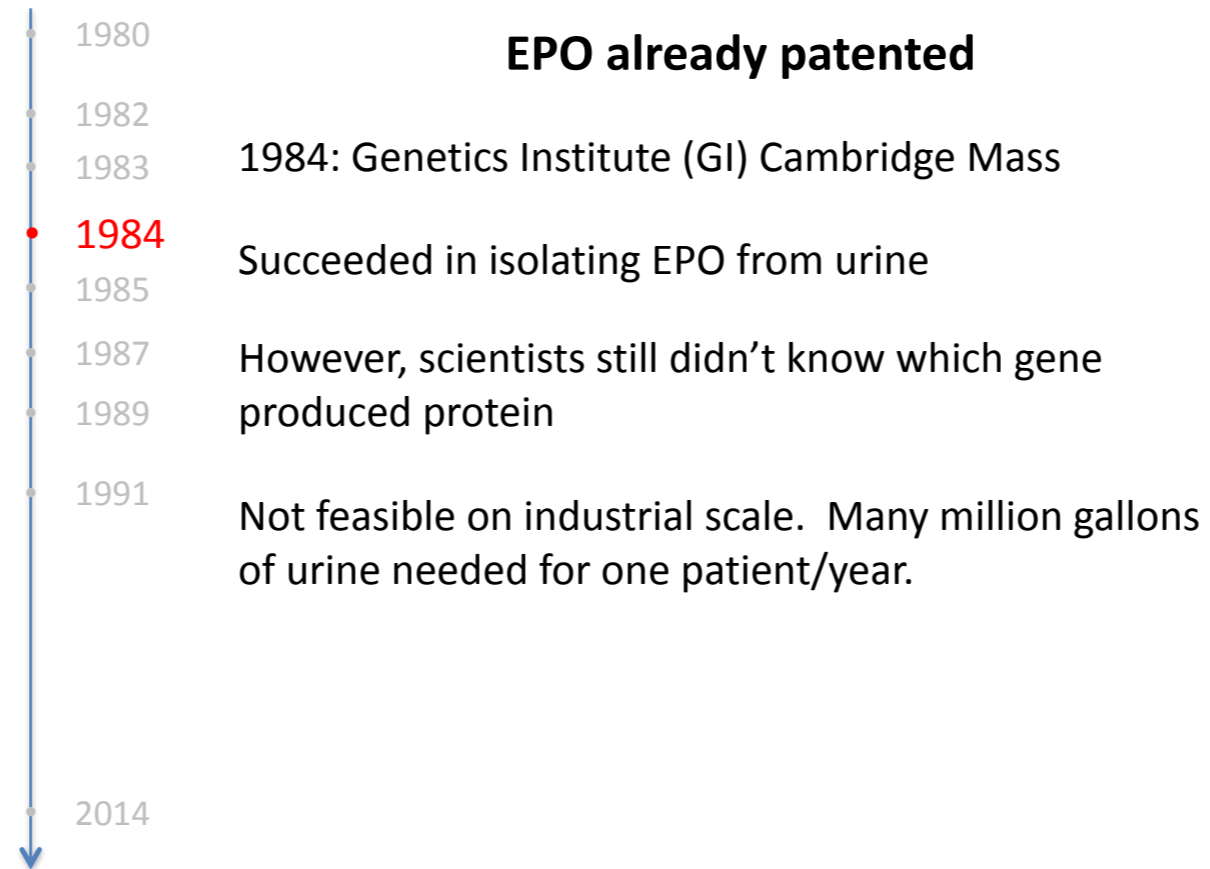
Product Patent

X No

Surprise. NOT! Anticipated



EPO already patented



AMGEN

What can Amgen Market?



Amgen: No patent on Product

GI: No way to produce in sufficient quantities

To produce, both cos. in patent infringement- Amgen no product, and GI would have to use some form of the Amgen's genetically modified cell patent

Years of legal battles for right to market EPO

10% of development cost for Epogen was legal bills



Success (?!)



1989: US FDA approves Epogen for market

Still unclear who can market what- legal stalemate continues



Epogen to market



1980
1982
1983 March 1990: Federal judge orders both GI and Amgen to exchange royalty-free cross-licenses on EPO. Neither could have 100% control of the market
1984
1985

1987
1989 Anyway, Amgen would go on to sell \$\$\$ Billions of Epogen over next 30 years.

1990

AND have a spring board to develop many other successful products

2014



Amgen Wins



Stock Appreciation 135,000% since IPO
\$10,000 investment at IPO would be valued at
\$13,500,000 today

2014





1-Sufficient financing raised in early stages allowed them to cover many years of cash burn so they didn't have to out-licensing technology/domestic distribution. Additionally the strategic pool of early investors and advisors gave them advantage/credibility/knowledge to succeed in risky new market.

2-Focused and well-managed R&D. Rathmann had a strategic focus on a handful of high-potential projects with large unmet medical need. Resources weren't wasted on unnecessary projects and were available when the company was ready to upscale its discovery. They could remain efficient and survive the approval process without compromising assets to bridge the period.

3- Key strategic partnership. Understanding early on the Amgen wasn't prepared to manufacture Epogen on their own, lead to the partnership with Kirin Brewery. The joint venture gave Amgen a head start on the market as soon as FDA approval received. Also allowed Amgen to segment the market geographically and by indication leading to Epogen being the leading treatment for chronic kidney disease and chemotherapy related Anemia.

