

IKEV-BOSFOR

**Biotech Market Penetration
Strategies
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Top Biotech Drug Sales

<i>Drug</i>	<i>Company</i>	<i>Disease</i>	<i>2004 sales (\$M)</i>	<i>2003 Sales (\$M)</i>
Epogen	Amgen	Anemia	2601	2435
Aranesp	Amgen	Anemia	2473	1544
Rituxan	Genentech	Non-Hodgkin Lymphoma	2326	1982
Enbrel	Amgen	Arthritis	1900	1300
Neulasta	Amgen	Neutropenia	1740	1256
Avonex	Biogen	Multiple Sclerosis	1417	1168
Neupogen	Amgen	Neutropenia	1175	1267
Rebif	Sereno	Multiple Sclerosis	1091	819
Synagis	MedImmune	Infectious Disease	942	849
Cerezyme	Genzyme	Gaucher Disease	839	739
Viread	Gilead	HIV	783	567
Gonal-f	Sereno	Infertility	573	526
Avastin	Genentech	Metastatic Colorectal Cancer	555	N/A
Herceptin	Genentech	Breast Cancer	483	425
Visudyne	QLT	Wet AMD	448	356
Provigil	Cephalon	Excessive Daytime Sleepiness	439	290
Renagel	Genzyme	End- Stage Disease	364	282
Actig	Cephalon	Breakthrough Cancer Pain	344	237
Erbix	imClone	Metastatic Colorectal Cancer	261	N/A
AmBisome	Gilead	Infectious Disease	212	198

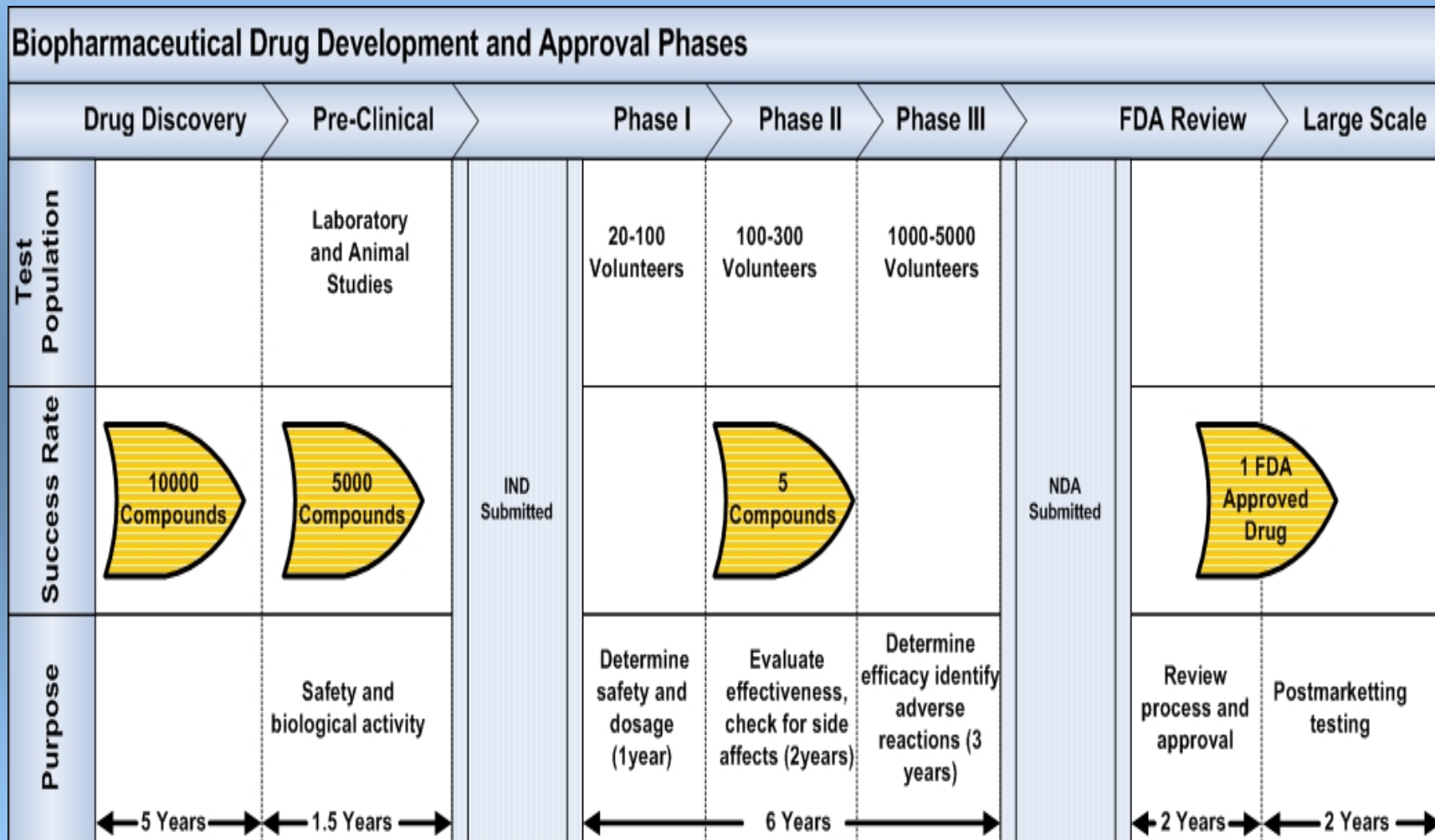
Why Biotech Drugs are Expensive?

- Extremely high *¹Pre-IND failure rate for *²NMEs
- 1 in 5 NMEs passes clinical trials
- Takes 10 years from IND to market
- Multiple review cycles
- Development Cost of per NME: ~ \$800 million
- High cost of clinical trials
- High cost of building biopharmaceutical manufacturing facility: \$150M to \$600M
- High cost of facility validation and approval.

*¹Pre-Investigational New Drug Application

*²New Molecular Entities

Drug approval Process



Biotech Market Penetration Strategies

- Acquire drug companies, with promising drug (Phase II & Phase III)
- Obtain a partnership in licensing agreement for regional production and selling rights of the drug.
- Outsource biopharmaceutical drug production.

**“TURKISH PHARMACEUTICAL COMPANIES
ARE NEW IN THE BIOTECH ARENA THUS
NEED AN EXPERT PARTNER”**

Why Outsource Biomanufacturing?

- Eliminate high cost of building facilities
- Avoid facility validation and approval
- Focus on core business initiatives
- Optimize and control operating cost
- Free resources
- Focus on core business initiatives
- Obtain high quality at low cost
- Reduce time-to market

Introduction to Celltrion's CMO Strategy

Capitalizing on its CMO business and manufacturing infrastructure, Celltrion aspires to be a leading global biopharmaceutical company



Facilities

Phase I



▪ Current Facility

1. Land Size

- 23 acres (Building: 287K ft²)

2. Capacity

- 50K Liter (12.5K X 4)

Phase II



▪ Expansion Facility

1. Land Size

- 24.5 acres (Building: 801K ft²)

2. Capacity

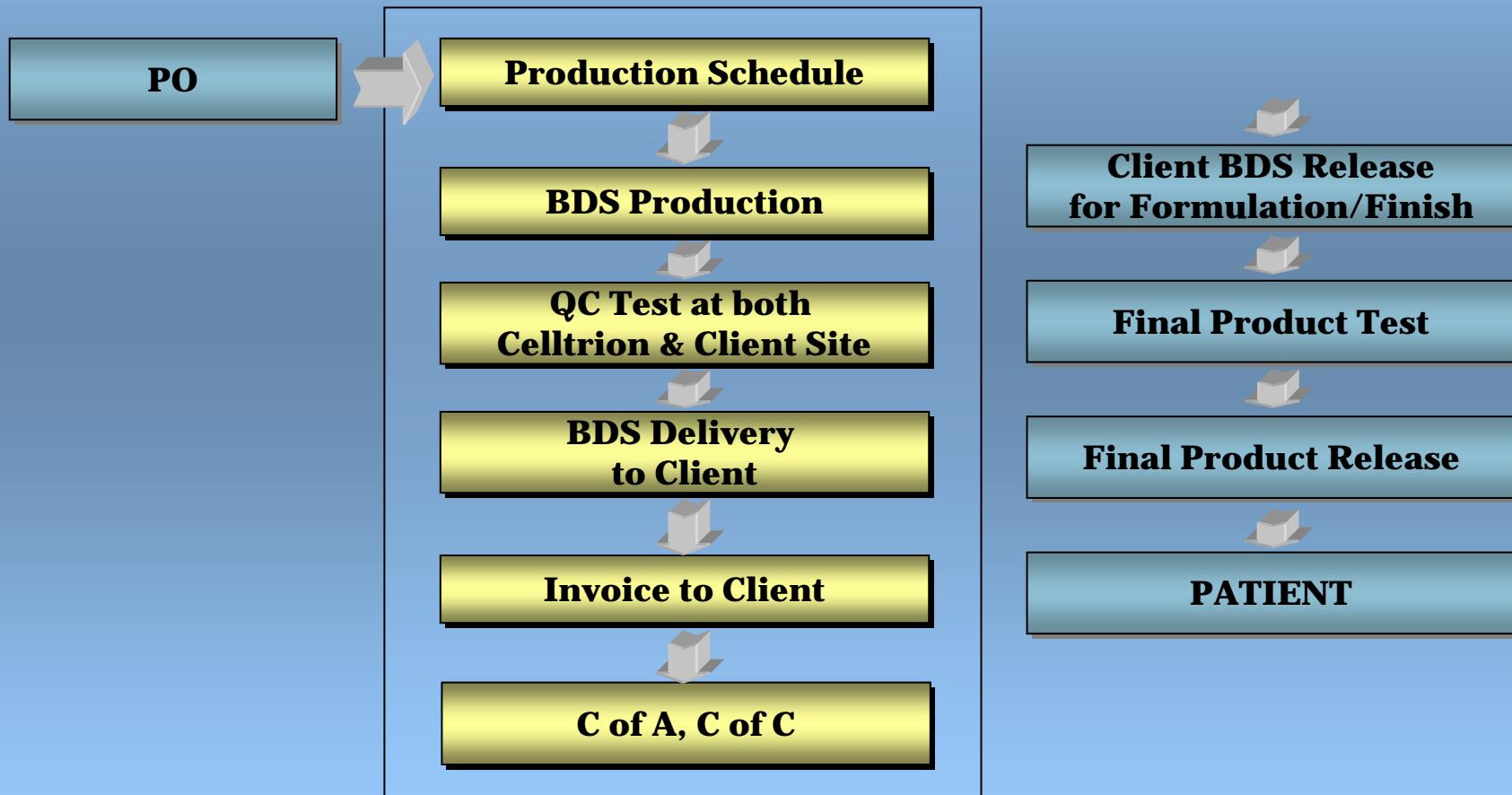
- 192K Liter (15K X 12, 3K X 4)

Celltrion's Production Capacity

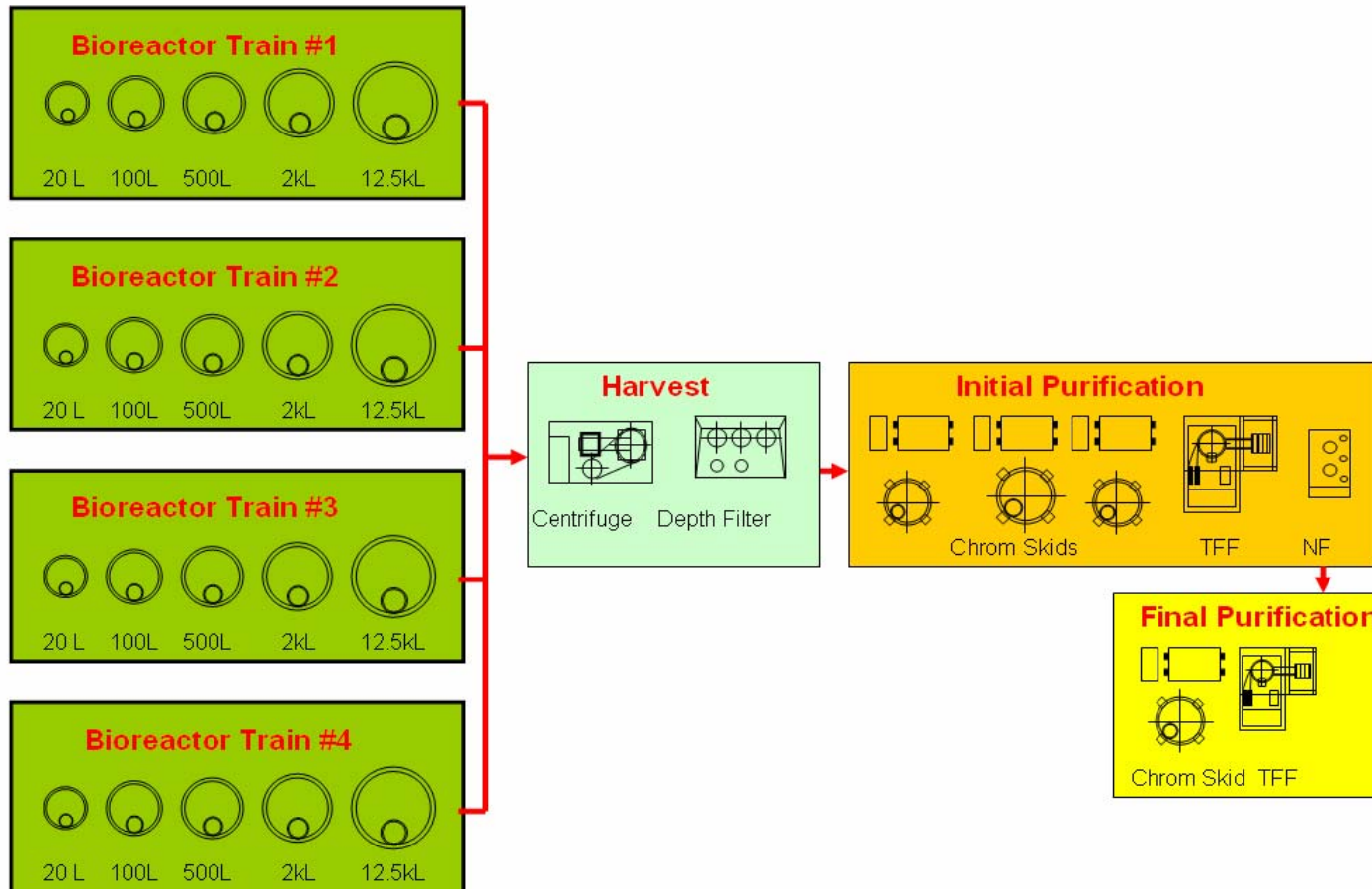
Facility	Capacity	Configuration	Facility Status	Location
Existing Facility	50,000 L	4 Trains X 12,500 L	Commercial Operation	Incheon, Site I
1st Expansion Facility	90,000 L	6 Trains X 15,000 L	Under Construction	Incheon, Site II
2nd Expansion Facility	90,000 L	6 Trains X 15,000 L	Planned	Incheon, Site II
Small-scale cGMP Facility	12,000 L	4 Trains X 3,000 L	Under Construction	Incheon, Site II
Total Capacity	242,000L			

Flow Chart of Contract Manufacturing

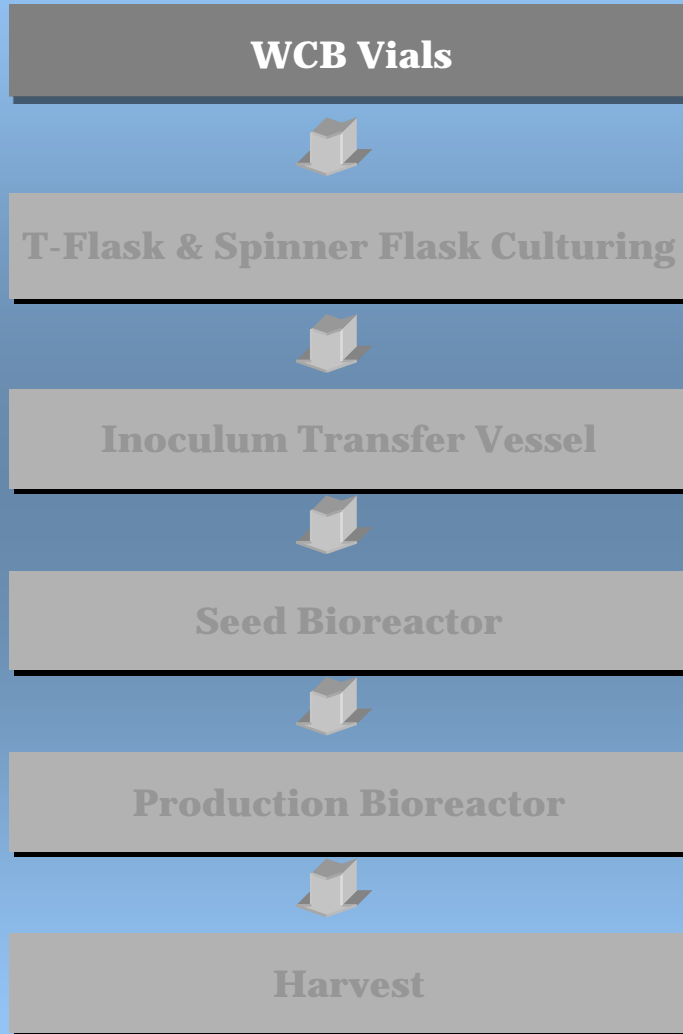
- **Rolling forecast from client**
- **Routine Procedure**



Process Flow



Typical Production Steps



LN2 Tank for WCB Storage

Cell Culture: Inoculum Preparation

WCB Vials



T-Flask & Spinner Flask Culturing



Inoculum Transfer Vessel



Seed Bioreactor



Production Bioreactor



Harvest



Weighing and Dispensing



Room Name	Weighing & Dispensing Area
Purpose	원료의 측량과 소분 작업 수행
Equipment Spec.	Floor scale 2대, Balance 5대, Drum lifter 2대, Booth & Hood 5대
Manufacturer.	Floor scale/Balance (Sartorius), Drum lifter (Servolift), Booth & Hood (녹십자 EM)

Media and Buffer Preparation



Room Name	Media/Buffer preparation Area
Purpose	세포 배양에 필요한 media 와 product 정제 과정에 필요한 buffer 제작
Equipment Spec.	Media prep. Tank (Fixed 3대), Buffer prep. Tank (7대)
Manufacturer.	BioEngineering

Cell Culture: Seed Bioreactors

WCB Vials



T-Flask & Spinner Flask Culturing



Inoculum Transfer Vessel



Seed Bioreactors



Production Bioreactor



Harvest



Seed Bioreactors

Cell Culture: Production Bioreactors

WCB Vials



T-Flask & Spinner Flask Culturing



Inoculum Transfer Vessel



Seed Bioreactor



Production Bioreactors



Harvest



**12,500 L
Bioreactors
(2 Floor)**



**12,500 L
Bioreactor
Sampling
(1 Floor)**

Harvest and Recovery

WCB Vials



T-Flask & Spinner Flask Culturing



Inoculum Transfer Vessel



Seed Bioreactor



Production Bioreactor



Harvest and Recovery



Centrifuge



Depth Filters

Purification: Chromatography



Chromatography Columns and Pumps

**4 Chromatography Steps:
- Diameters from 1.2 ~ 1.6 m**



Purification: Ultrafiltration & Diafiltration

TFF (Tangential Flow Filtration) Equipment



2 TFF Steps:

- membrane areas 5 ~ 15 m²