

université  
PARIS-SACLAY

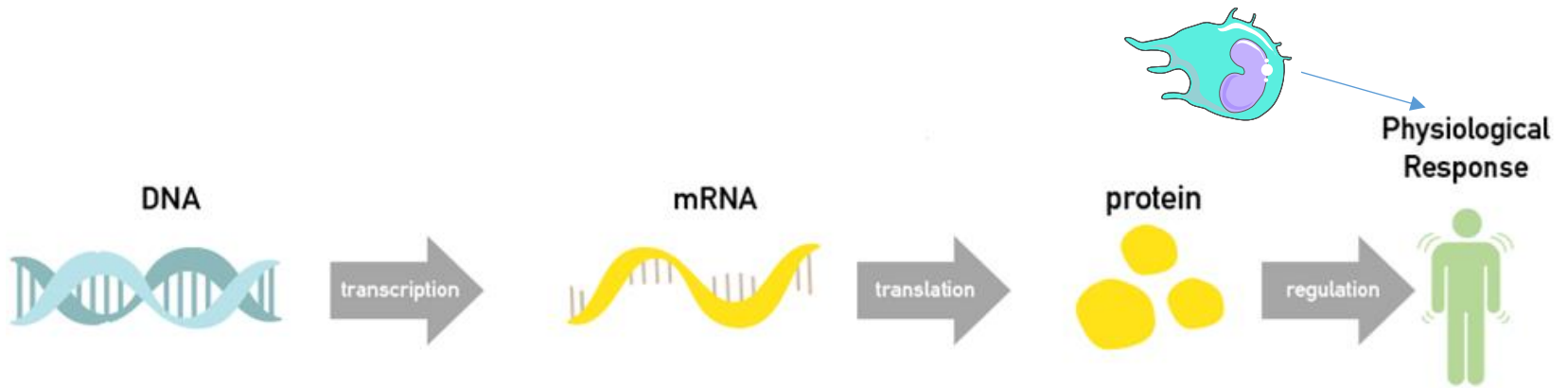
FACULTÉ DE  
PHARMACIE

# TU08 Biotechnology

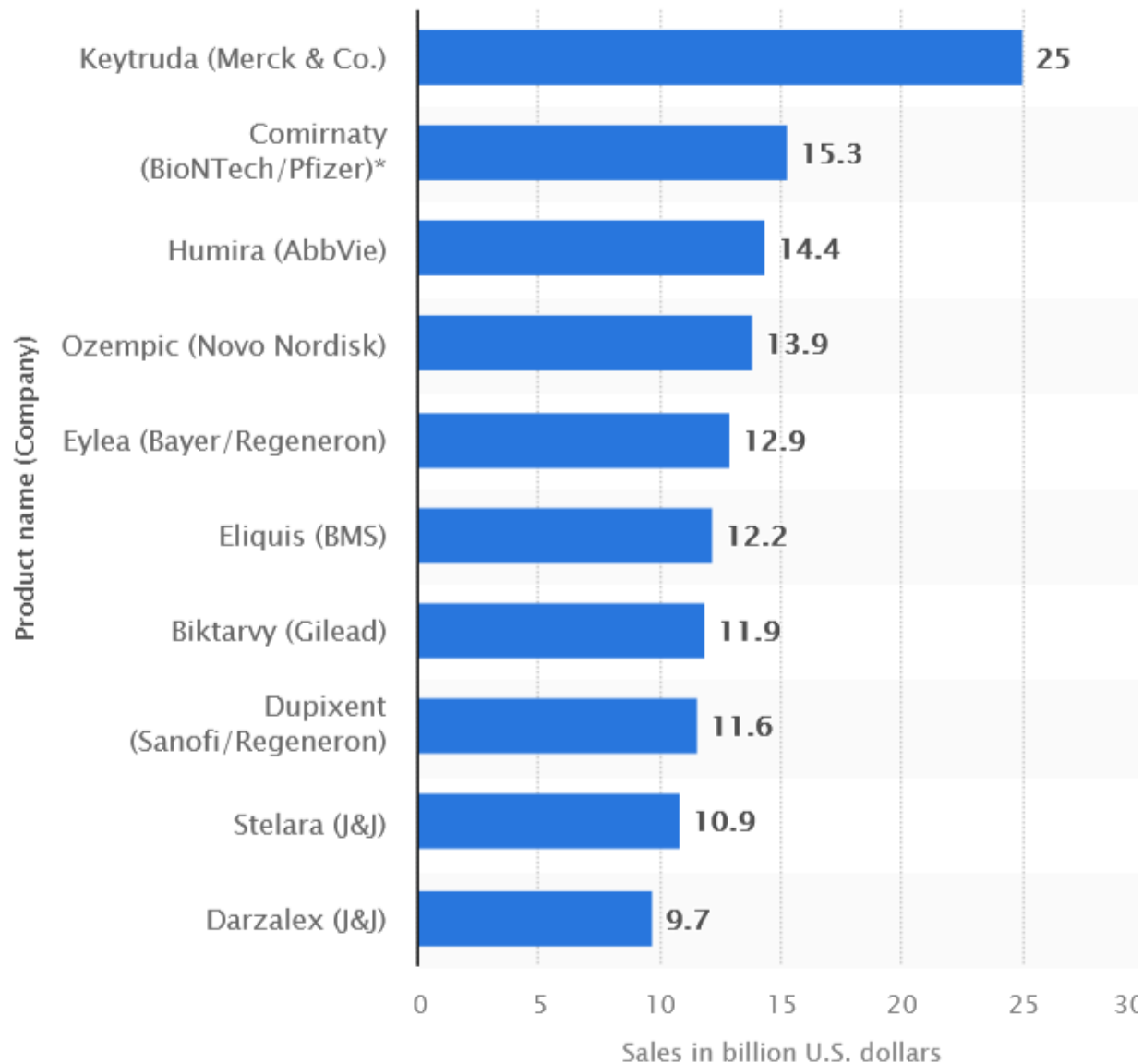
Dr. Francois Fay  
Assistant Professor  
Institut Galien Paris-Saclay



# Bio-pharmaceuticals



# Top 10 Best-Selling Drugs of 2023



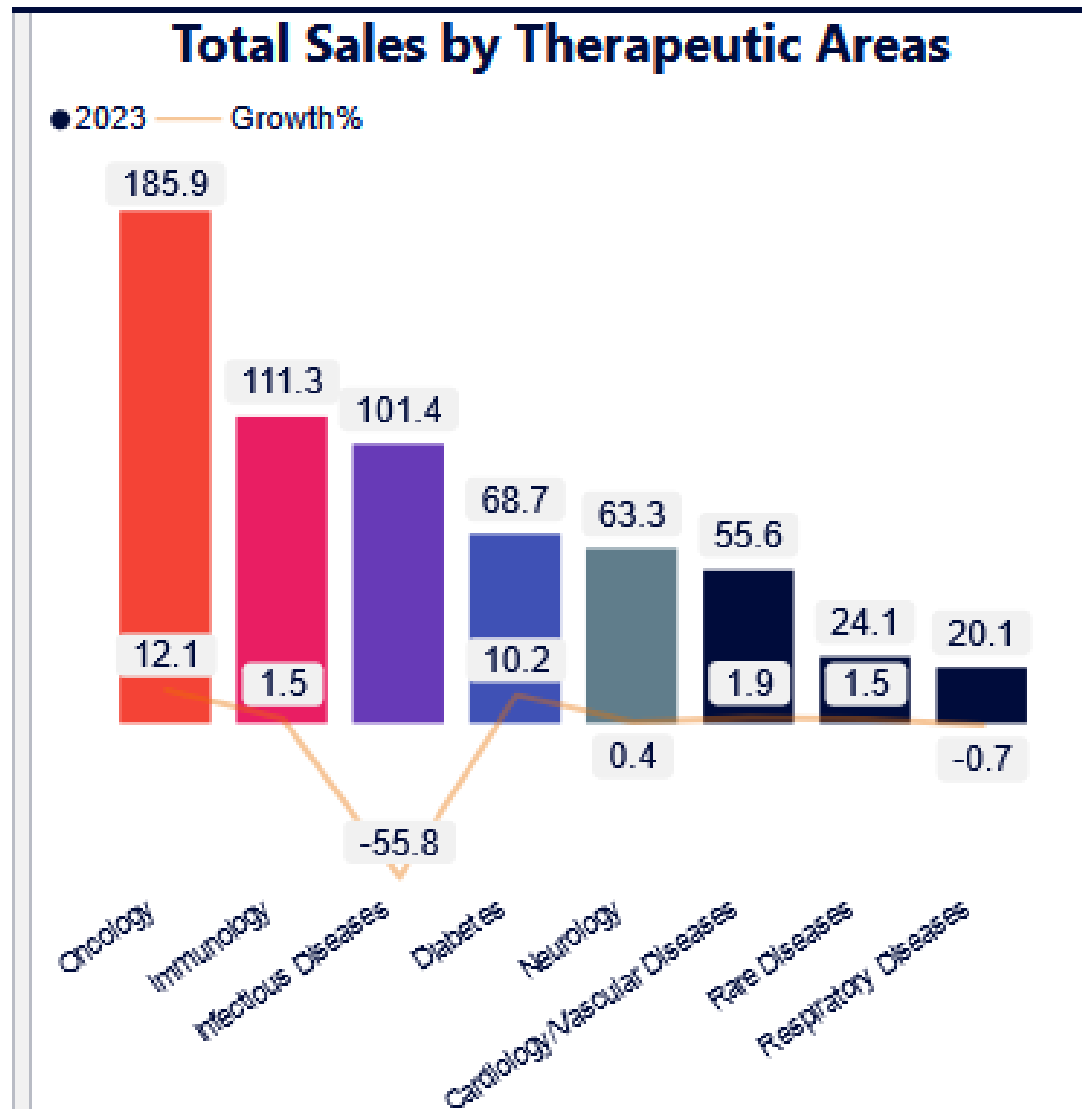
# Top 10 Best-Selling Drugs of 2024 (anticipated)

**Table 1 | Top product forecasts for 2024**

Rank	Product	Company	Pharmacological class	2024 worldwide sales forecast (US\$)
1	Keytruda	Merck & Co.	Anti-PD1 mAb	27.19 billion
2	Ozempic	Novo Nordisk	GLP1 receptor agonist	16.13 billion
3	Dupixent	Sanofi/Regeneron	Anti-IL-4/IL-13 mAb	13.45 billion
4	Eliquis	Bristol Myers Squibb/Pfizer	Factor Xa inhibitor	13.31 billion
5	Biktarvy	Gilead Sciences/Yuhan	HIV INSTI/NRTI/NtRTI	12.57 billion
6	Darzalex	Johnson & Johnson	Ant-CD38 mAb	11.98 billion
7	Opdivo	Bristol Myers Squibb/Ono	Anti-PD1 mAb	11.33 billion
8	Comirnaty	Pfizer/BioNTech	SARS-CoV-2 vaccine	10.79 billion
9	Gardasil	Merck & Co./CSL	HPV vaccine	10.03 billion
10	Skyrizi	AbbVie	Anti-IL-23 mAb	9.93 billion

Forecasts include sales booked by global marketing partner, where relevant. Estimates based on sellside equity analyst models, compiled by Evaluate Pharma to generate a consensus view. INSTI, integrase strand transfer inhibitor; GLP1, glucagon-like peptide 1; HPV, human papilloma virus; mAb, monoclonal antibody; NRTI, nucleoside reverse transcriptase inhibitor; NtRTI, nucleotide reverse transcriptase inhibitor; PD1, programmed cell death protein 1; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2. Source: EvaluatePharma and company statements. December 2023.

# Top 10 Best-Selling Drugs of 2023



## MOST EXPENSIVE DRUGS IN THE US MARKET IN 2023

<b>\$3.0M</b> Cost per dose	 <b>HEMGENIX</b> <small>etranacogene desaparivovec dltb</small>		<b>\$1.07M</b> Cost per year	 <b>Zokinvy</b> <small>(lonafamib)</small>	
	<b>Hemophilia B</b> Gene therapy			<b>Hutchinson-Gilford progeria syndrome</b> Small molecule drug	
<b>\$3.0M</b> Cost per dose	 <b>skysona</b>		<b>\$1.01M</b> Cost per year	 <b>DANYELZA</b>	
	<b>Cerebral adrenoleukodystrophy</b> Gene therapy			<b>Relapsed or refractory high-risk neuroblastoma</b> Biologic drug	
<b>\$2.8M</b> Cost per dose	 <b>zynteglo</b>		<b>\$0.97M</b> Cost per year	 <b>KIMMTRAK</b>	
	<b>Transfusion-dependent thalassemia</b> Gene therapy			<b>Uveal melanoma</b> T-cell therapy	
<b>\$2.25M</b> Cost per dose	 <b>zolgensma</b>		<b>\$0.85M</b> Cost per treatment	 <b>LUXTURNA</b>	
	<b>Spinal muscular atrophy</b> Gene therapy			<b>Biallelic RPE65-mediated inherited retinal disease</b> Gene therapy	
<b>\$1.26M</b> Cost per year	 <b>myalept</b>		<b>\$0.84M</b> Cost per year	 <b>FOLOTYN</b> <small>(pralatrexate injection)</small>	
	<b>Leptin deficiency</b> Biologic drug			<b>Relapsed or refractory peripheral T-cell lymphoma</b> Small molecule drug	

Source: <https://www.fiercepharma.com/special-reports/priciest-drugs-2023>

# Bio-pharmaceuticals

?

# Bio-pharmaceuticals

## EMA:

Biological medicines (also called “biopharmaceuticals”) are comprised of **proteins** such as hormones (growth hormones, insulins, erythropoietins), **enzymes** that are naturally produced in the human body, or **monoclonal antibodies**, but also **blood products**, immunological medicinal products such as sera and **vaccines**, **allergens**, and **advanced technology products** such as **gene** and **cell therapy** products.

*A Consensus Information Document “Process on Corporate Responsibility in the Field of Pharmaceuticals”*



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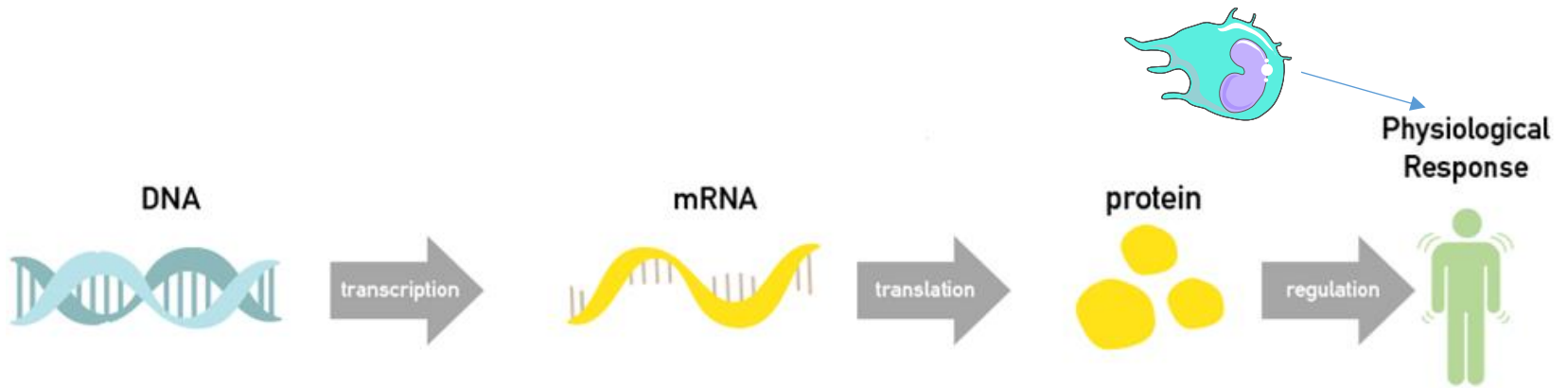
*A Consensus Information Document “Process on Corporate Responsibility in the Field of Pharmaceuticals”*

## FDA :

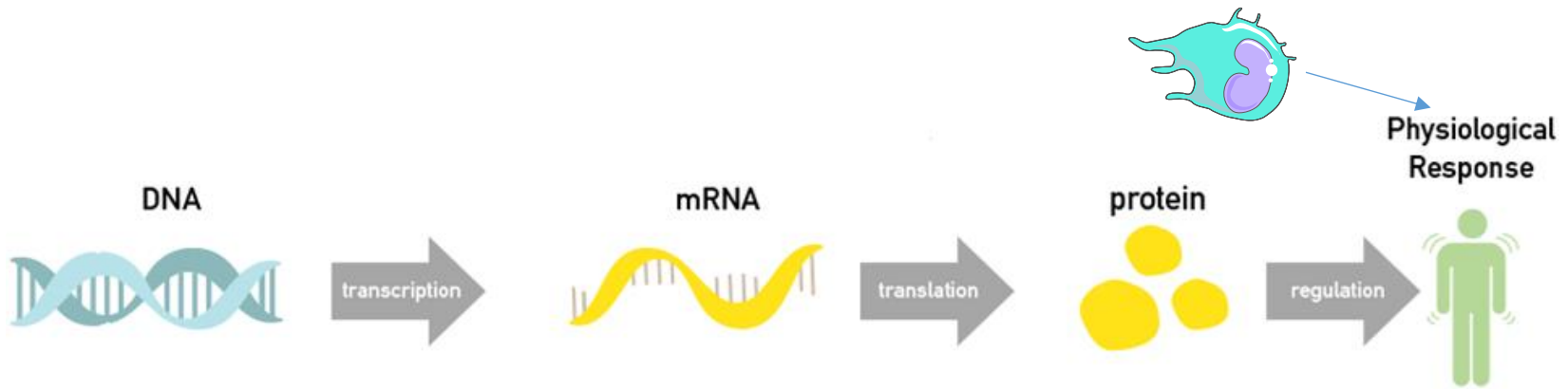
### What is a biological product?

Biological products include a wide range of products such as **vaccines**, **blood** and **blood components**, **allergens**, **somatic cells**, **gene therapy**, **tissues**, and **recombinant therapeutic proteins**. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other cutting-edge technologies.

# Bio-pharmaceuticals



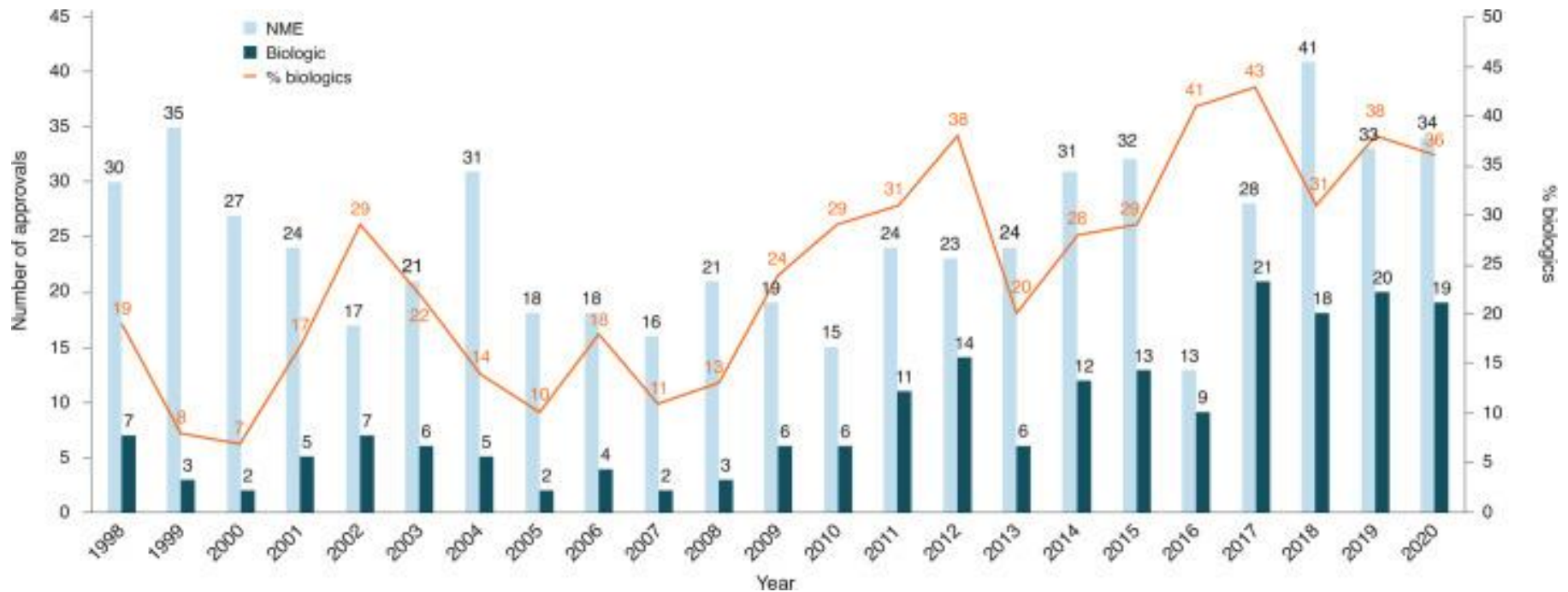
# Bio-pharmaceuticals



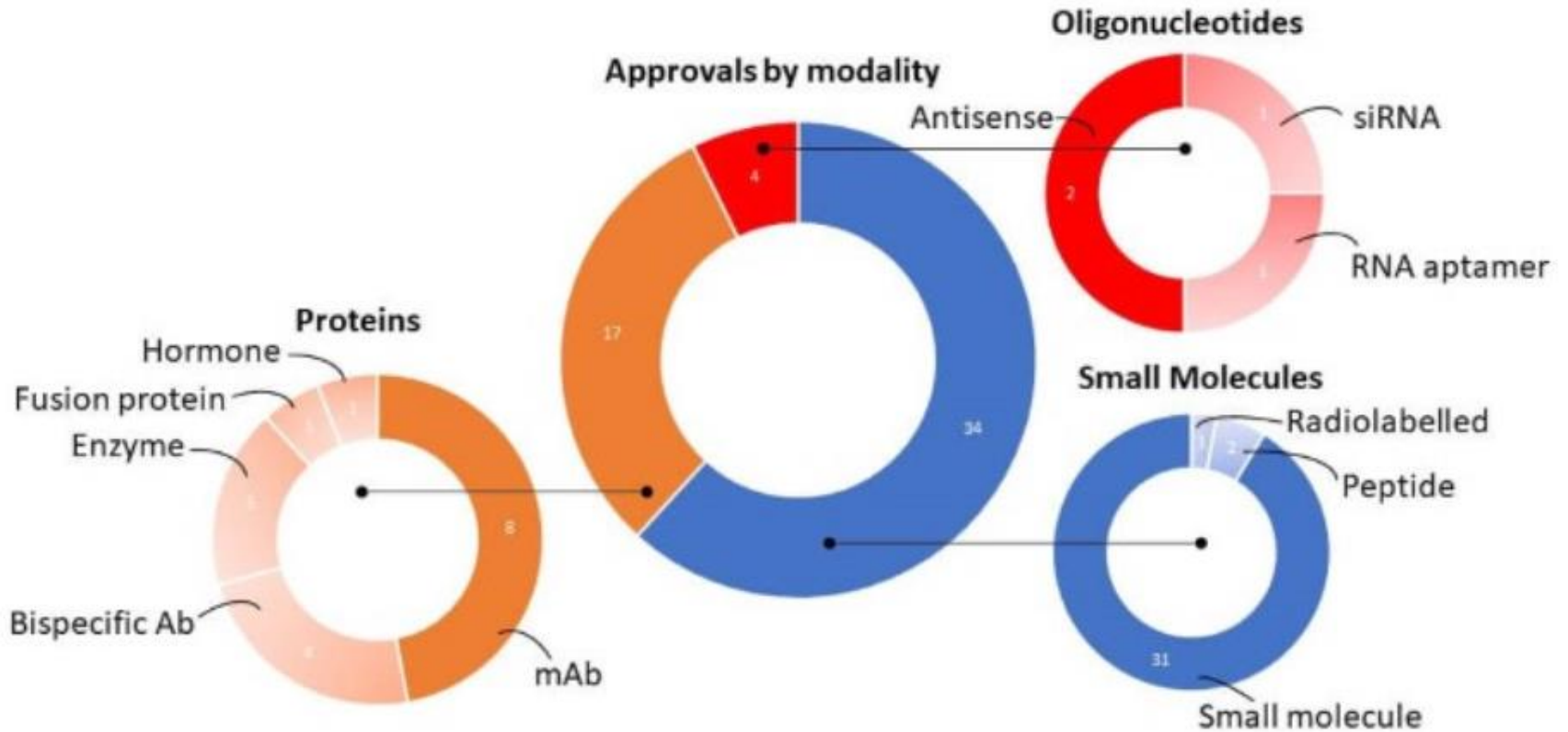
**≈ 350 biologics are commercially available**

# Evolution

## New chemical entities and biologics approved by the FDA



# Biologics in 2023

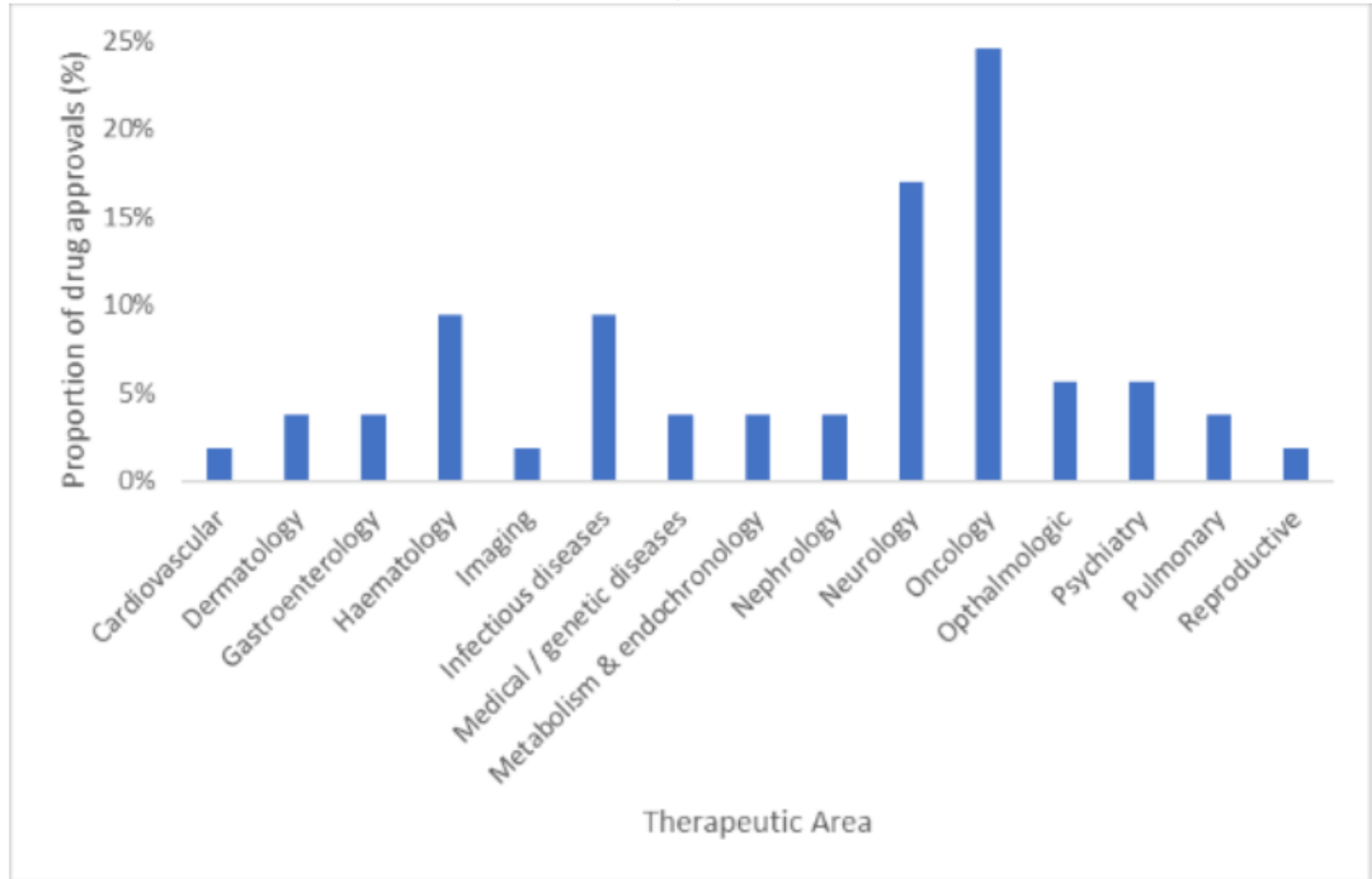


*Adapted from Muller A, 2023 FDA approvals Nature Reviews in Drug Discovery, Jan 2024.*

# Biologics *now*

## FDA 2018 - 2019

FDA Approvals by Therapeutic Area



Adapted from Muller A, 2023 FDA approvals *Nature Reviews in Drug Discovery*, Jan 2024.



# Biologics *now*

## FDA 2018 - 2019

### Some examples of biologics authorized by the FDA in 2019



Vyondys 53
(golodirsen)
antisense oligonucleotide
targets DMD gene exon 53
treatment of Duchenne muscular dystrophy
30 mg/kg IV once a week
Sarepta

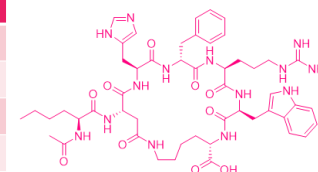


Reblozyl
(luspatercept-aamt)
ActRIIb-IgG recombinant fusion protein
TGF- $\beta$ inhibitor
treatment of anemia from beta thalassemia
1 mg/kg subcutaneously once every 3 weeks
Celgene/Acceleron

Evenity
(romosozumab-aqqg)
humanized monoclonal antibody
sclerostin inhibitor
treatment of osteoporosis in high-risk women
210 mg subcutaneously once a month
UCB (acq. Celltech)



Vyleesi
(bremelanotide)
synthetic $\alpha$ -MSH peptidomimetic
melanocortin receptor agonist
treatment of HSDD in premenopausal women
1.75 mg subcutaneously
AMAG/Palantin



Beovu
brovacizumab-dblb
humanized single-chain antibody
VEGF-A inhibitor
treatment of wet AMD
6 mg intravitreally once a month
Novartis/Alcon (acq. ESBATech)



Scenesse
(afamelanotide)
synthetic $\alpha$ -MSH peptidomimetic
Melanocortin receptor agonist
for erythropoietic protoporphyria
delivered by subcutaneous implant
Cilnuvel

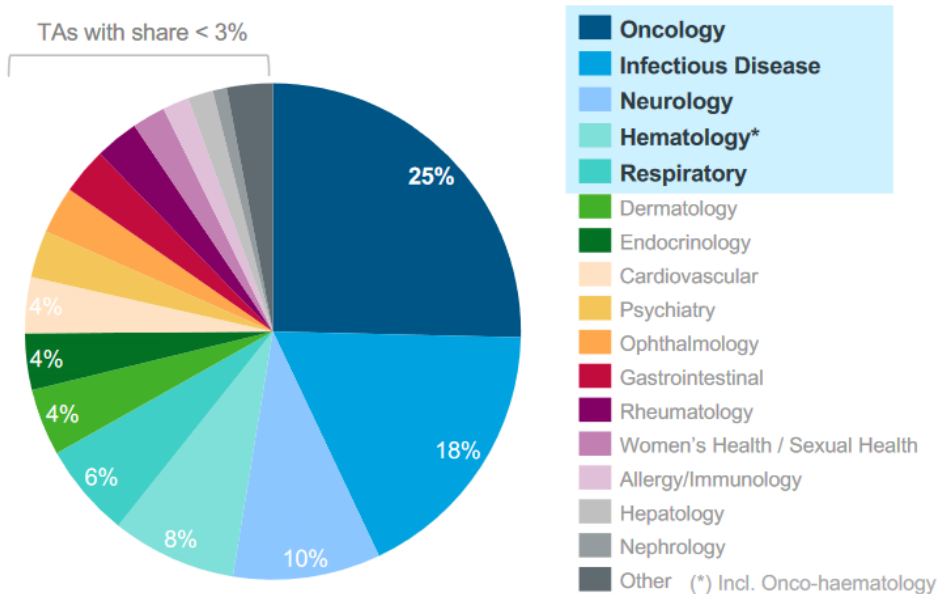




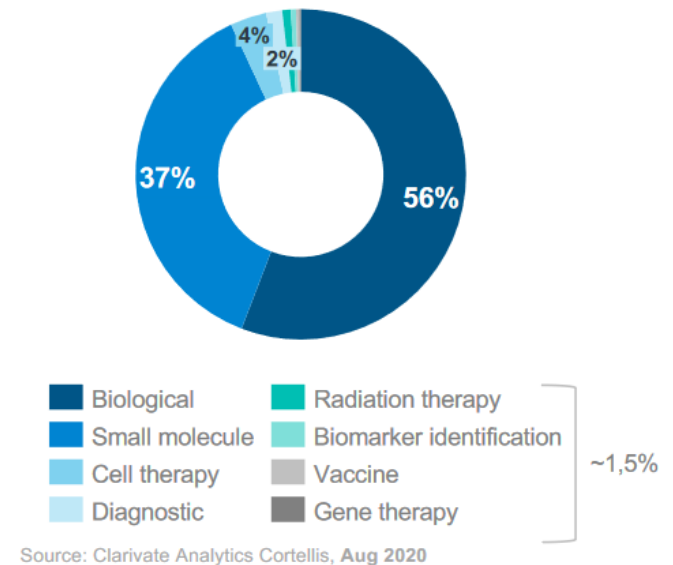
# Biologics in the future?

European clinical trials started in 2020

Pipeline summary – key therapeutic areas<sup>2</sup> [# trials started in 2020]



Key categories



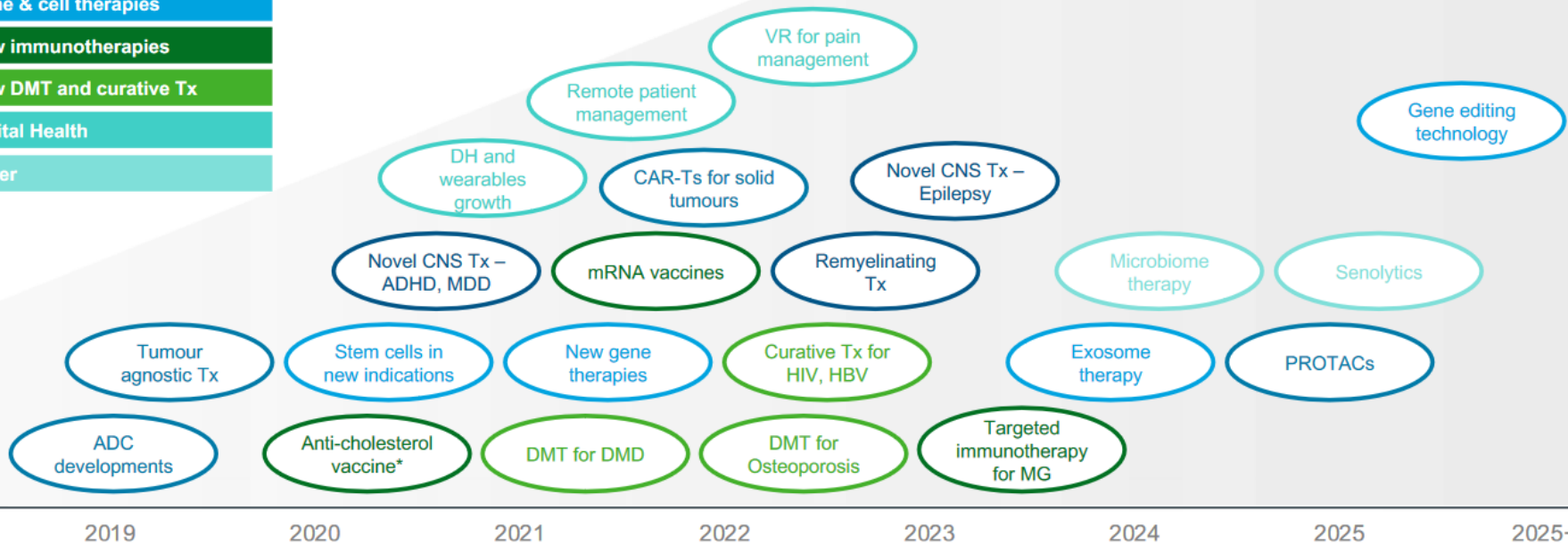
# Biologics in the future?

## High-level overview of new innovation areas coming to the market in the 5-year perspective

### Key:

Novel CNS therapies
Novel technologies in Oncology
Gene & cell therapies
New immunotherapies
New DMT and curative Tx
Digital Health
Other

Illustrative



**Abbreviations:** Disease modifying therapies (DMTs), therapies (Tx), Digital health (DH), virtual reality (VR), central nervous system (CNS), attention deficit hyperactivity disorder (ADHD), major depressive disorder (MDD), human immunodeficiency virus (HIV), hepatitis B virus (HBV), Proteolysis Targeting Chimeras (PROTAC), Chimeric antigen receptor T cells (CAR-Ts), antibody drug conjugate (ADC), Myasthenia Gravis (MG) - [link](#) to glossary Source: [IQVIA analysis](#)

# Economics

## Biologic Drugs in the US Market

**2%**

Biologics account for 2% of total prescription drug volume in the US.

**37%**

Biologics account for 37% of total prescription drug spend in the US.

**\$125.5 Bn**

Public and private insurers in the US spent \$125.5 billion on biologics in 2018.

**26**

The number of biosimilars approved in the US (as of Feb. 3, 2020).

Source: Joint Statement of the US Food & Drug Administration and the US Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace, February 3, 2020.

# Economics

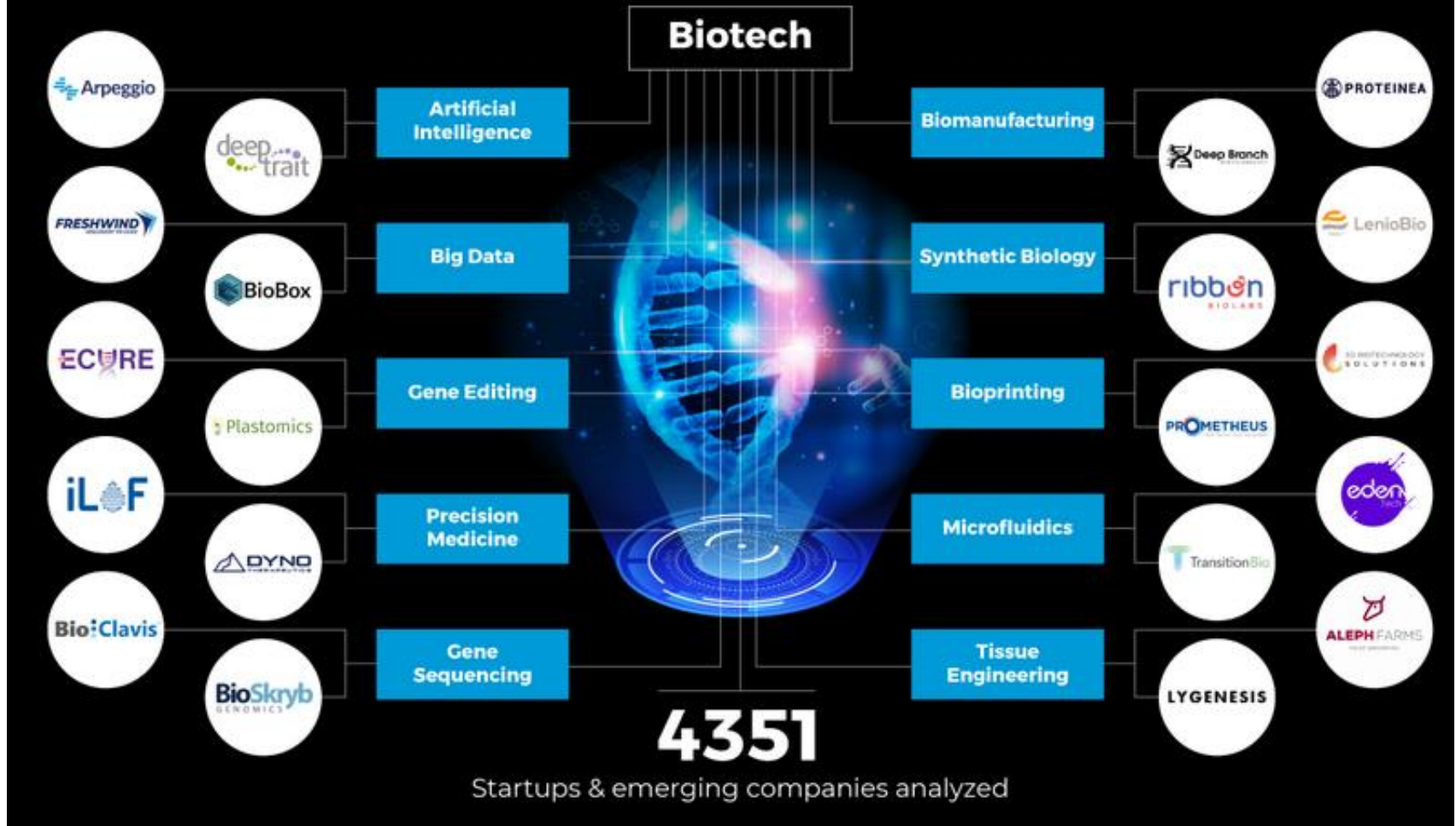
## Big pharma

### TOP 20 BIOPHARMA COMPANIES BASED ON 2023 TOTAL REVENUE



# Economics Trends

## Top 10 BioTech Trends & Innovations in 2025

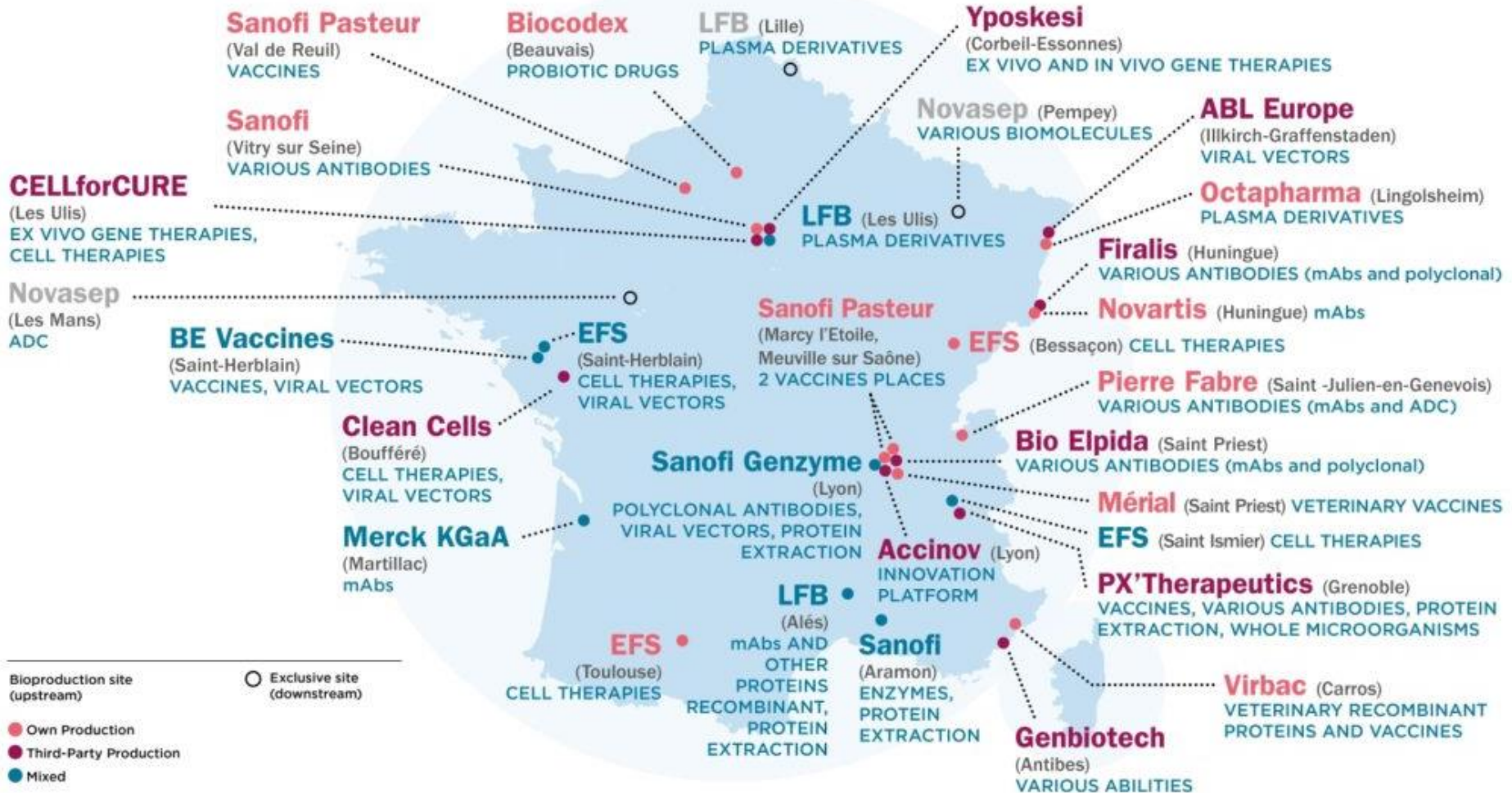




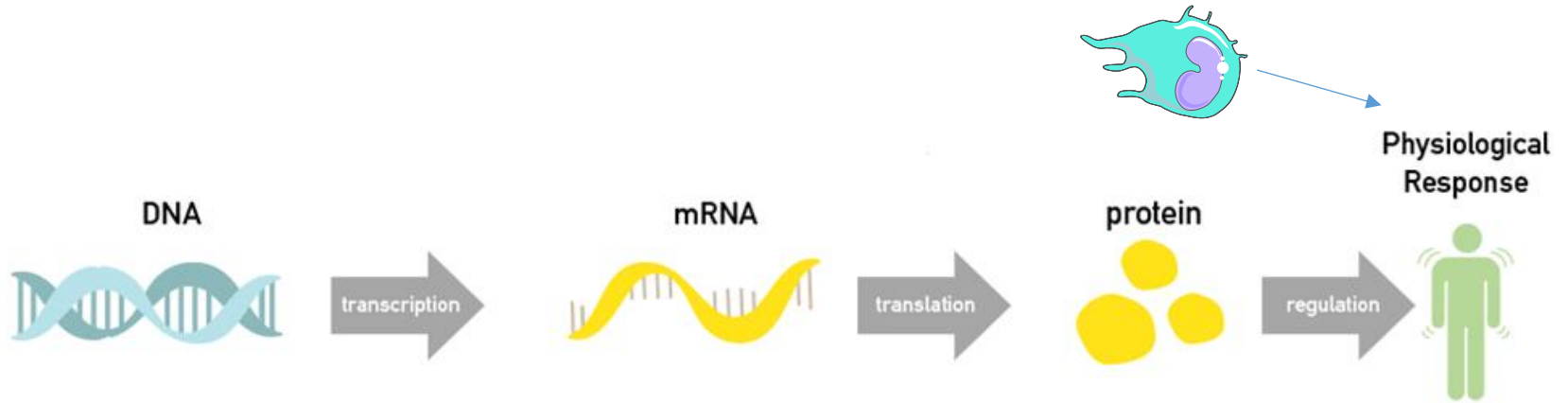
# Economics

## Biotech in France

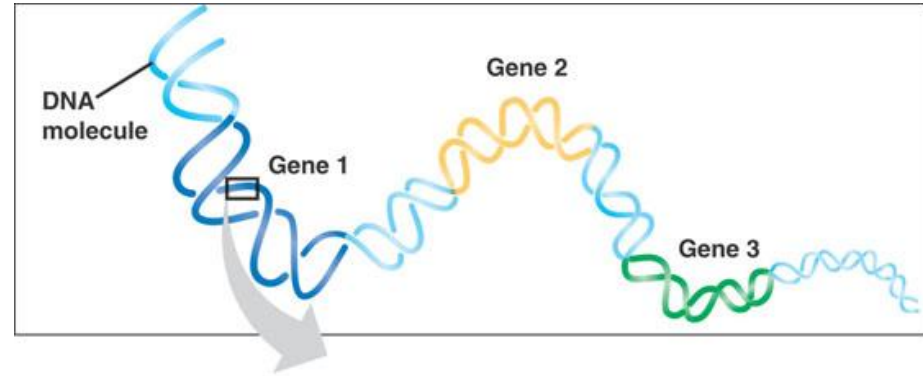
### 32 SITES OF PRODUCTION OF BIOLOGICAL MATERIALS IN FRANCE



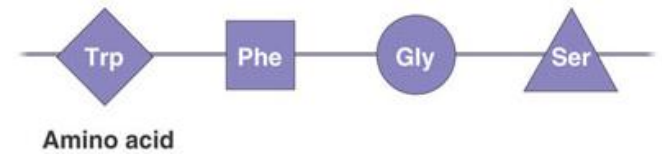
# Break



# From Gene to Protein(s)

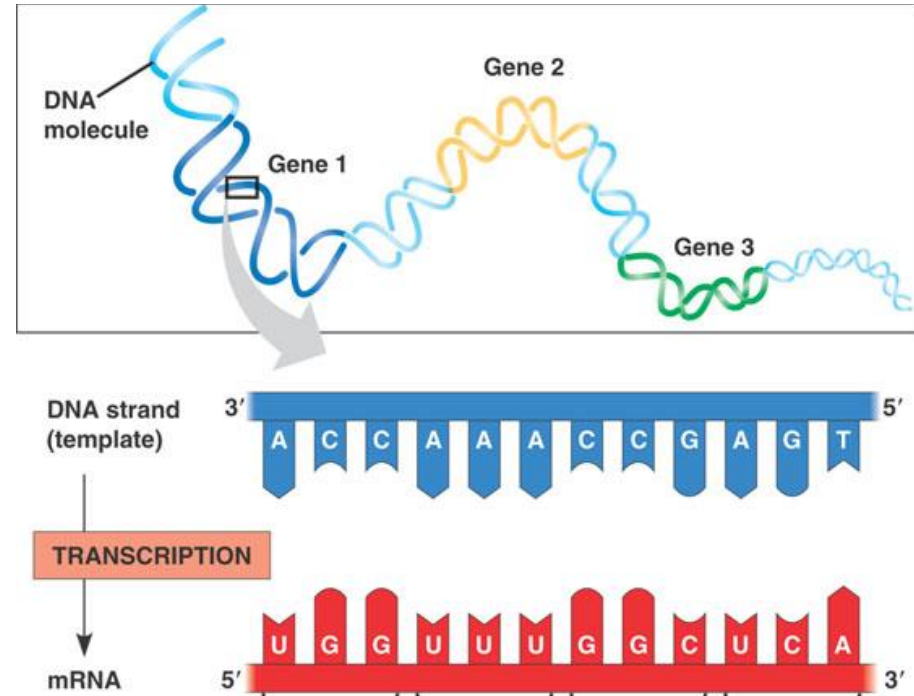


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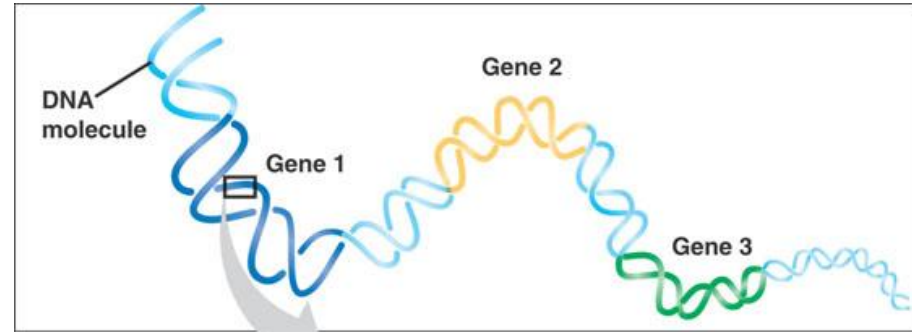
# From Gene to Protein(s)



## Transcription:

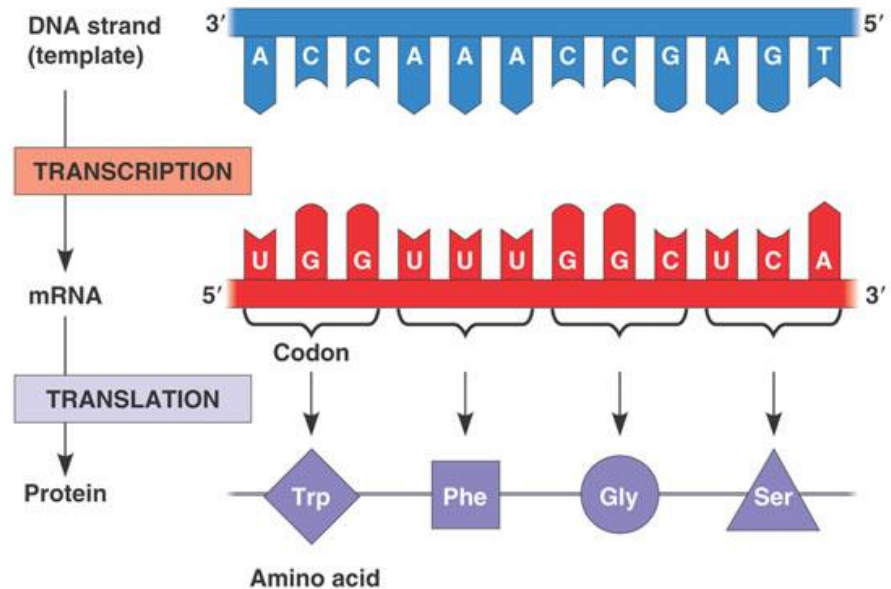
The synthesis of RNA under the direction of DNA, produces messenger RNA (mRNA)

# From Gene to Protein(s)

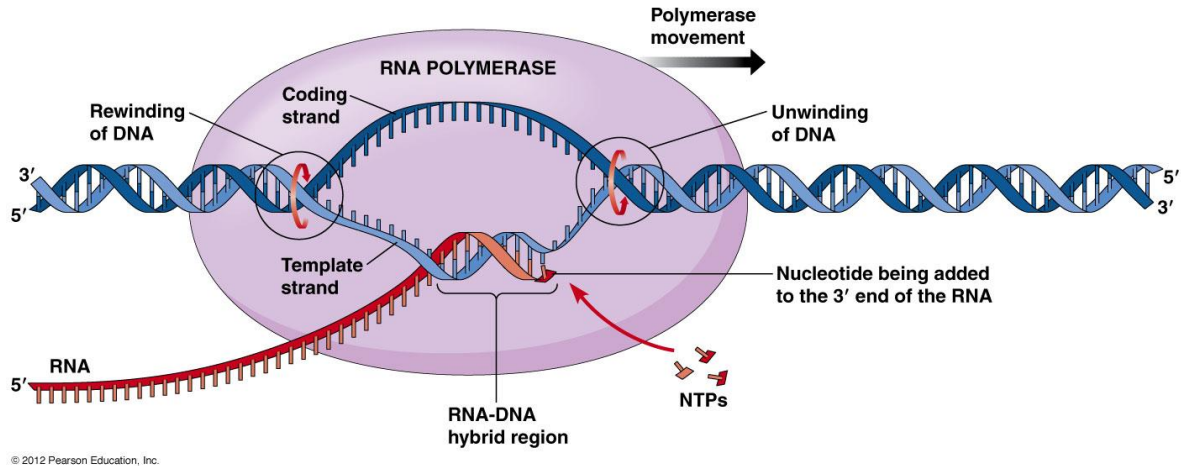


**Transcription:** The synthesis of RNA under the direction of DNA, produces messenger RNA (mRNA)

**Translation:** Synthesis of polypeptides under the direction of mRNA



# Transcription



**Initiation:** RNA polymerase, binds to **promoter DNA sequence**, and separate the two strands of the DNA helix (breaking the hydrogen bonds).

**Elongation:** Phosphate-RNA nucleotides (complementary to DNA strand) are added to the RNA strand following a 5' → 3' direction.

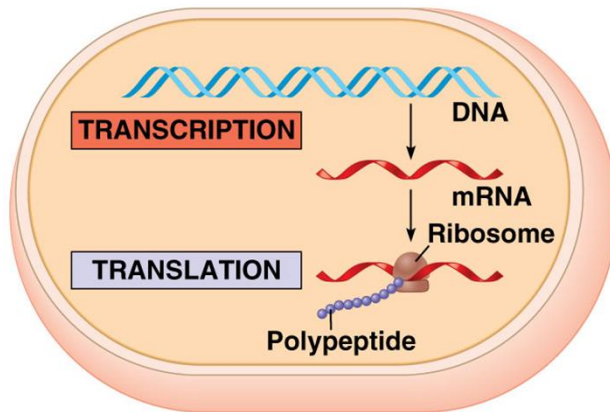
**Termination:** RNA polymerase transcribes a **terminator DNA sequence**, then mRNA and polymerase detach:

Eukaryotes, RNA produced is now called **pre-mRNA**

Prokaryotes = mRNA ready for use

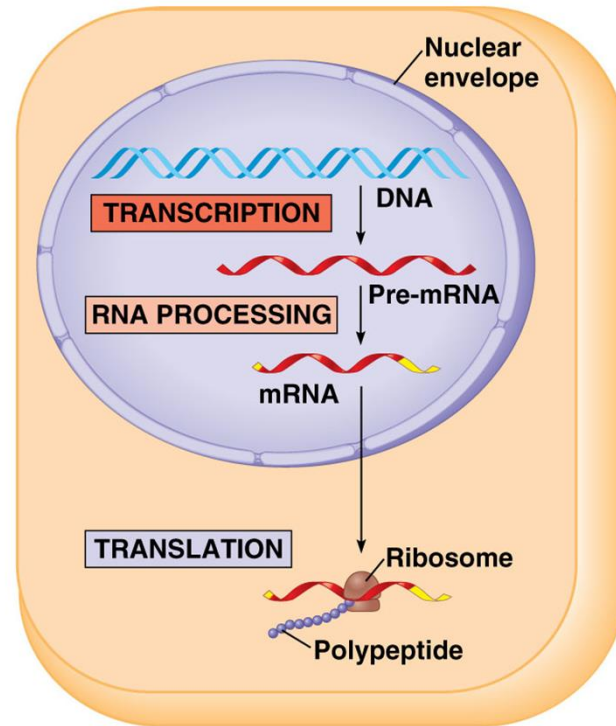
<https://www.youtube.com/watch?v=XzVXhemtwmA&index=4&list=PL3MAPgqN8JWib86aCRPB6hPcIMvJqR975>

# Location of the transcription and translation processes



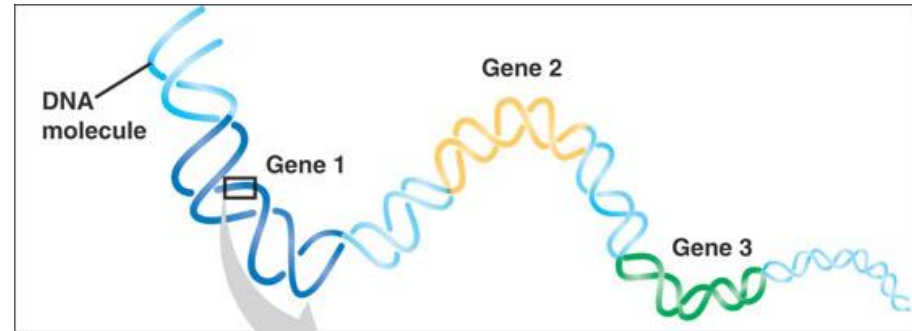
(a) Bacterial cell

© 2011 Pearson Education, Inc.



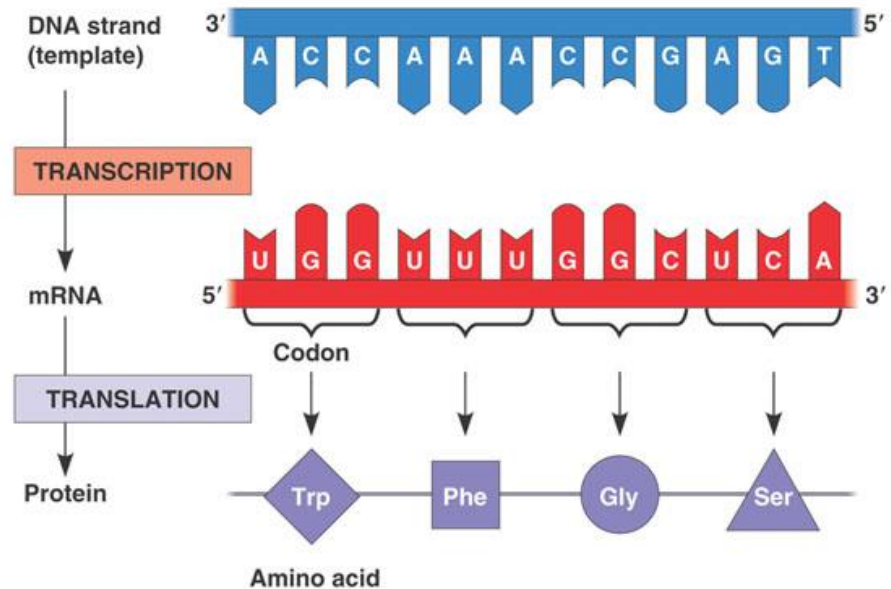
(b) Eukaryotic cell

# From Gene to Protein(s)

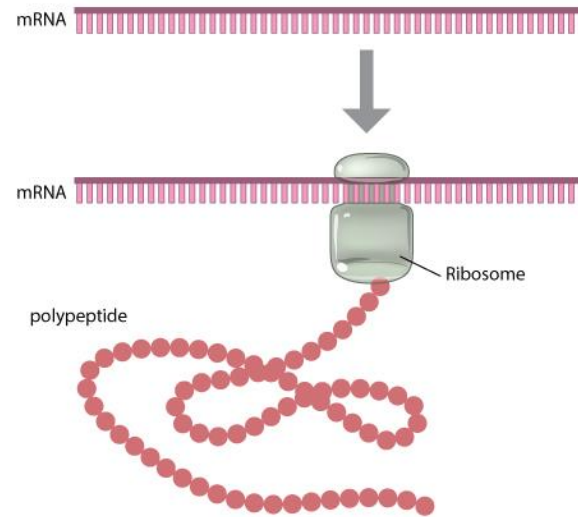


**Transcription:** The synthesis of RNA under the direction of DNA, produces messenger RNA (mRNA)

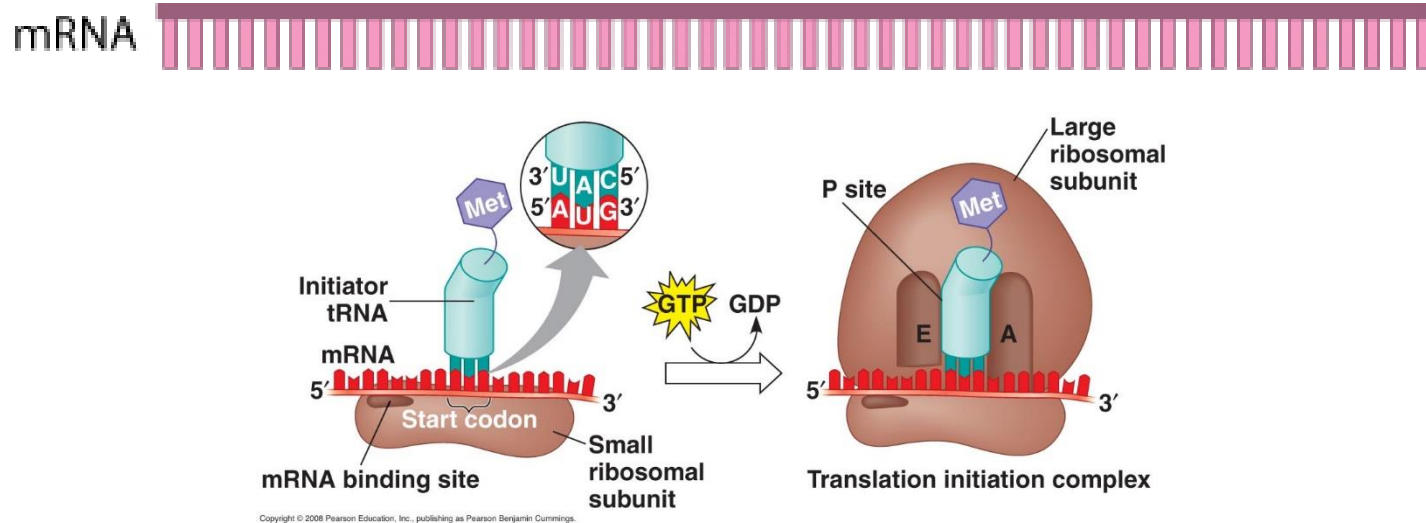
**Translation:** Synthesis of polypeptides under the direction of mRNA



# Translation



# Translation

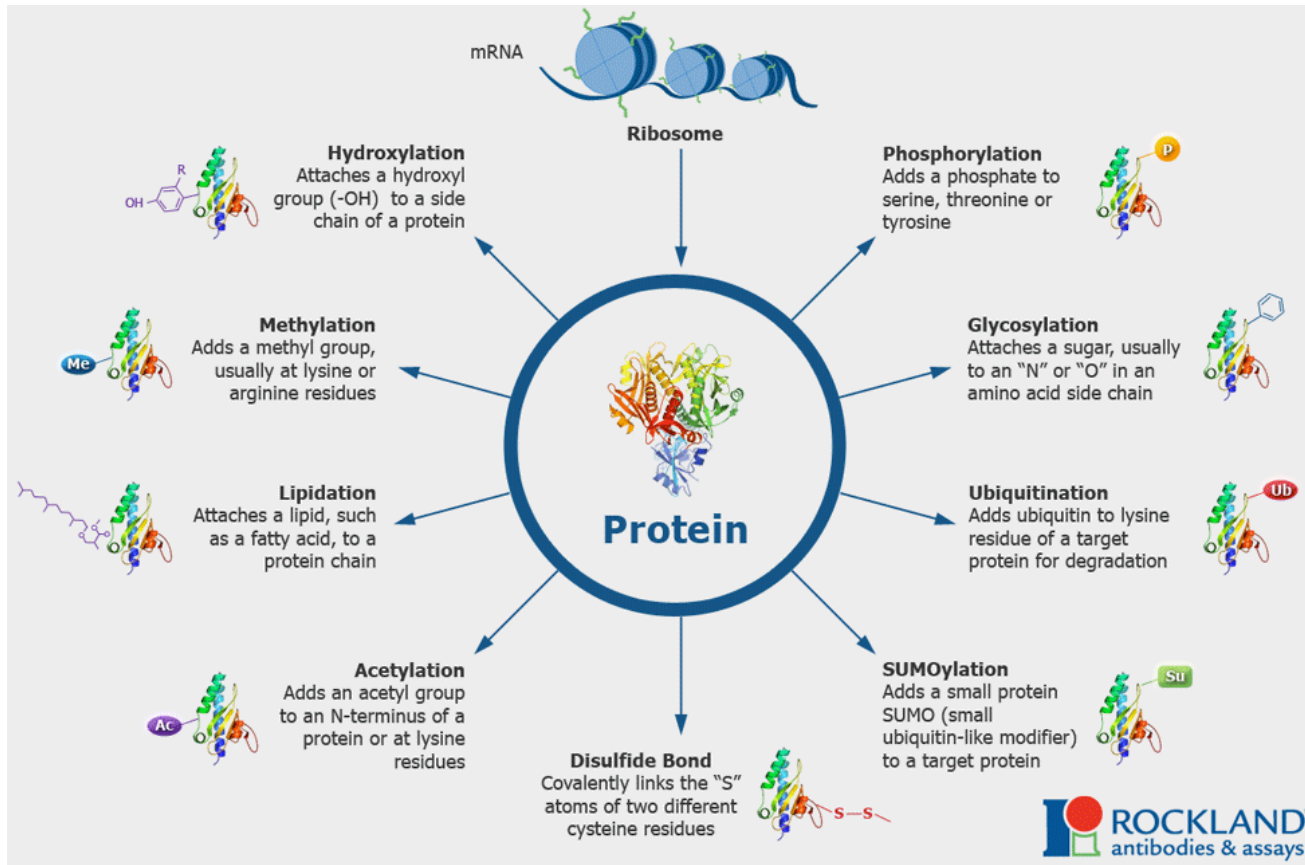


The ribosome assembles around the target mRNA:

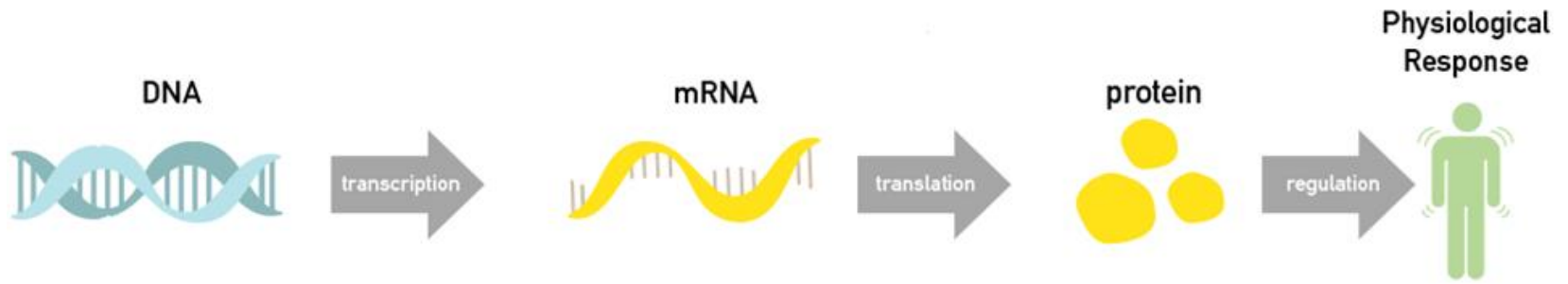
- Small subunit binds to start codon on mRNA (*The start codon always codes for the AA methionine/ the most common start codon is AUG*).
- tRNA carrying AA attaches to P site
- Termination occurs when specific sequences\* (called **stop codon**) are reached. (*\*sequences that not have complementary tRNA*)

# Post-translational modification(s)

Polypeptides may undergo **post-translational modification**, generally through enzymatic modification, to form the mature protein product.







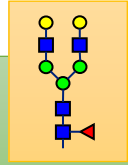
# Characteristics of Biologics

**Chemicals**

**Peptides**

**Non-glycosylated proteins**

**Glycosylated Proteins**



Aspirine

0,18kDa



Calcitonine

~3,5 kDa



Filgrastim

~19 kDa



Somatropin

~22 kDa

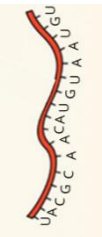


Epoietin

~30 kDa



Antibodies  
~150 kDa



iRNA ~ 10 kDa

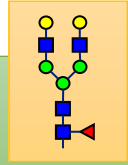
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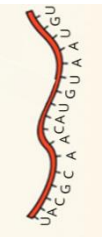


Epoietin

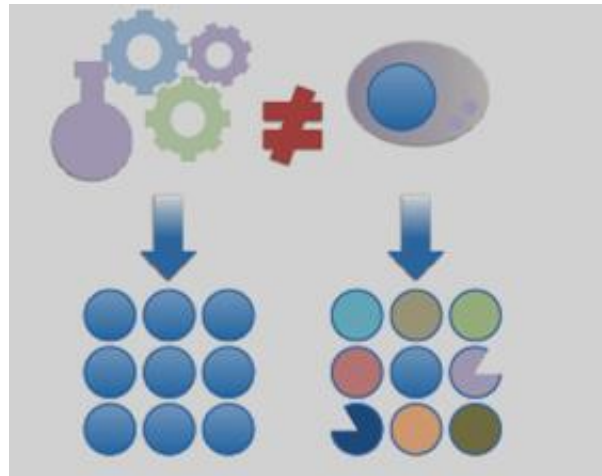
~30 kDa



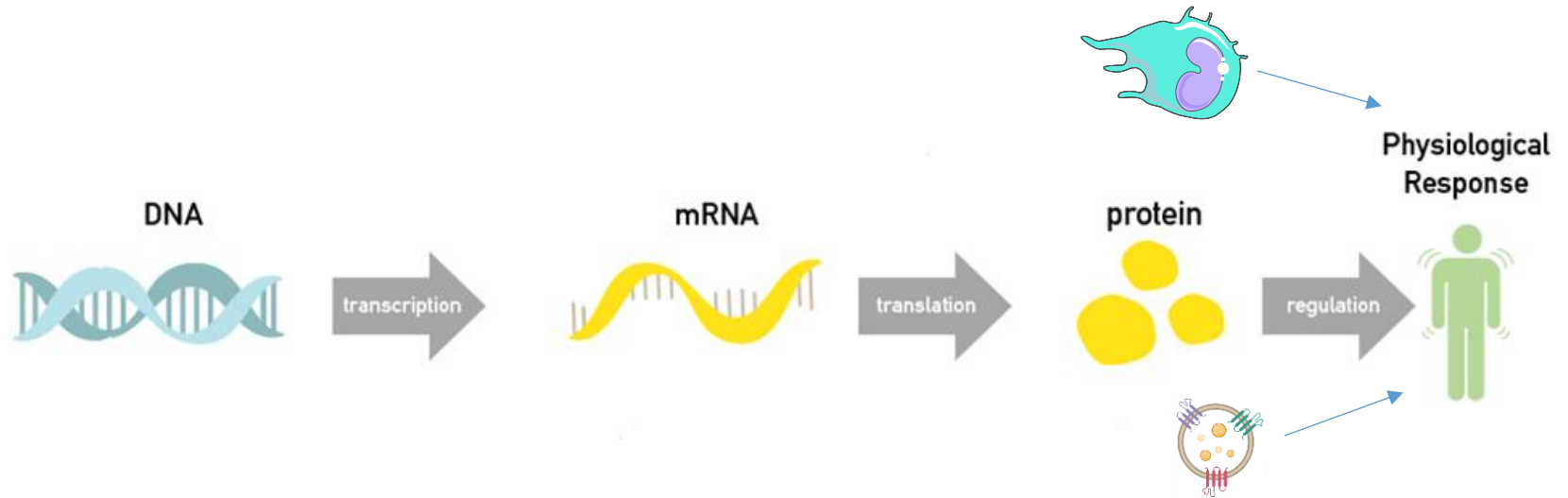
Antibodies  
~150 kDa



iRNA ~ 10 kDa



# Break



15/10/2024	TU 08: Biotechnology	09:00	12:15	Introduction to biotechnology (F Fay)
	TU 08: Biotechnology	14:00	17:00	Molecular tools in biotechnologies – an overview (F Gesbert)
17/10/2024	TU 08: Biotechnology	14:00	17:00	Proteins (I Turbica)
18/10/2024	TU 08: Biotechnology	09:00	12:15	Quality control 1 (M Taverna / C Smadja)
	TU 08: Biotechnology	14:00	17:00	oligonucleotide (F Fay)
22/10/2024	TU 08: Biotechnology	14:00:00	17:00	Gene therapy non viral vectors (F Fay)
23/10/2024	TU 08: Biotechnology	09:30	12:30	vaccines (I Turbica)

24/10/2024	TU 08: Biotechnology	09:15	12:15	EV (S Obeid)
	TU 08: Biotechnology	14:00	16:00	Plasma therapeutic Proteins (D. Bataille)
25/10/2024	TU 08: Biotechnology	09:00	12:15	Biobetters (M Taverna)
29/10/2024		14:00	15:00	Cell therapie (N Chaput)
06/11/2024	TU 08: Biotechnology	09:00	12:15	Quality control 2 (M Taverna / C Smadja)
		14:00	15:30	Viral vectors (D. Bonte)
		15:45	17:15	Application of gene transfer using viral vectors (E. Morel)

# Nice summaries

[http://www.wiley.com/college/test/0471787159/biology\\_basics/animations/fromGeneToProtein.swf](http://www.wiley.com/college/test/0471787159/biology_basics/animations/fromGeneToProtein.swf)

<http://www.nature.com/scitable/topicpage/translation-dna-to-mrna-to-protein-393>