Biotech & Pharma

Figures current as of October 2026

How medicines are discovered, tested, made, sold, and priced; the modalities and the therapeutic areas from obesity to cancer; genetic medicine, vaccines, and global health; China's rise and AI in discovery; the regulators and the pricing wars; devices and diagnostics; and where the industry stands.

MODULE 1 — Foundations: What a Drug Is

Goal: Establish the modalities, the mechanisms, and the industry's scale.

Small molecules and biologics, the modalities in a table, how drugs act on their targets, why genetic evidence improves the odds, and the industry's scale.

MODULE 2 — From Lab to Market

Goal: Follow a drug through discovery, trials, and approval with the numbers.

Discovery, the phases with their success rates and costs, the FDA's fast lanes including the new priority vouchers, the approval counts, and what happens after approval.

MODULE 3 — The Industry: Big Pharma and Biotech

Goal: Map the companies and the ecosystem.

The largest companies in a table, the biotech financing cycle and the 2026 reopening of the IPO market, and the three geographic centers.

MODULE 4 — The Chain Beneath: Manufacturers, Generics, and Middlemen

Goal: Profile the industry the public never sees.

Contract manufacturers and the BIOSECURE law, generics and biosimilars, the pharmacy benefit managers (PBMs) and the 2026 reform law, and where a $1,000 prescription's money goes.

MODULE 5 — The Patent Cliff and the Business Model

Goal: Explain the economics that drive everything else.

Exclusivity and the blockbuster, the cliff drug by drug, Humira's patent thicket and succession, the deal wave, and a licensing deal worked from both sides.

MODULE 6 — GLP-1 and the Obesity Revolution

Goal: Cover the largest drug story of the decade.

The drugs in a table, the mechanism and the trials, Lilly's lead and the pills, the next generation, falling prices, Medicare's bridge program, and the effects beyond medicine.

MODULE 7 — Cancer

Goal: Cover the largest therapeutic area.

The approaches in a table, immunotherapy and the ivonescimab challenge argued from both sides, conjugates, the 2026 pills, cell therapy, and cancer vaccines.

MODULE 8 — Heart, Metabolic, and Kidney Disease

Goal: Cover the diseases that kill the most people.

Statins to the first PCSK9 pill, the failed first test of lipoprotein(a) and what remains of the hypothesis, the SGLT2 accident, new drugs for blood pressure and kidney disease, and the convergence.

MODULE 9 — Immunology and Inflammation

Goal: Cover the franchise business.

The diseases and drugs in a table, Humira's succession, the drug classes and the move to pills, TL1A, and the setbacks in multiple sclerosis.

MODULE 10 — Genetic Medicine

Goal: Assess the therapies that edit, replace, or silence genes.

CRISPR from Casgevy and the edited babies to editing inside the body, gene therapy's paradox argued, the Elevidys case, RNA drugs, and the access problem.

MODULE 11 — Vaccines and mRNA

Goal: Cover the technology that ended a pandemic and the policy turn against it.

The COVID vaccine race and its distribution failure, the collapse and the first mRNA flu vaccine, the US policy upheaval and the court's stay argued from both sides, and the vaccine business.

MODULE 12 — Neuroscience and the Hard Diseases

Goal: Cover the areas where the industry has struggled.

Aduhelm and the antibodies that followed, the amyloid dispute, new mechanisms in psychiatry and neurology, non-opioid pain, and rare disease.

MODULE 13 — Infectious Disease and Global Health

Goal: Cover the medicines for the diseases of the poor and the defenses against the next pandemic.

HIV, tuberculosis, and malaria in a table, lenacapavir's rollout, the funding collapse argued from both sides, antimicrobial resistance, and pandemic preparedness.

MODULE 14 — China's Rise

Goal: Explain how China became the second biotech superpower.

The licensing numbers in a table, how the industry was built, the deal structures, and whether China is a threat or a solution, argued from both sides.

MODULE 15 — AI in Drug Discovery

Goal: Assess what artificial intelligence has and has not done for medicine.

AlphaFold and the Nobel, the companies in a table, the honest scorecard, and the verdict so far.

MODULE 16 — The Regulators

Goal: Explain who decides what is a medicine, and who checks them.

The FDA, its 2025-26 turmoil argued from both sides, Vioxx and OxyContin, the other regulators, and the debate over surrogates and accelerated approval.

MODULE 17 — Pricing, Policy, and Access

Goal: Cover the pricing wars and the global access question.

Why the US pays more, the instruments of 2025-26 in a table, the pricing war argued from both sides, the insulin case, Europe and the rest, and access.

MODULE 18 — Devices and Diagnostics

Goal: Cover the other half of medical technology.

The device industry and its technologies in tables, diagnostics and the Galleri trial argued, and the regulatory divide.

MODULE 19 — Where Things Stand, and What to Watch

Goal: Close with the argument, the contradictions, and a dated watch list.

Five forces reshaping the industry, who checks it, seven contradictions, the signals of late 2026 to 2028, and a last word.

The State of the Art, as of October 2026

The Leading Medicines and Tools, and Who Makes Them

This table is the course's reference point: the leading or newest product in each part of the field as of October 9, 2026, who makes it, when it was approved or what its status is, and the module that explains it. A few terms recur. A modality is a kind of drug, such as a pill, an antibody, or a gene therapy (Module 1). The FDA is the US Food and Drug Administration, which approves medicines (Module 16), and Phase III is the last and largest stage of human trials before a company files for approval (Module 2).

Category	Leading or newest product	Maker	Approved or status	Module
Obesity, injected	Zepbound (tirzepatide)	Eli Lilly	Approved November 2023	6
Obesity, pill	Wegovy pill (oral semaglutide); Foundayo (orforglipron)	Novo Nordisk; Eli Lilly	Approved December 22, 2025 and April 1, 2026	6
Diabetes	Mounjaro (tirzepatide); the weekly insulins Awiqli and Onswik	Eli Lilly; Novo Nordisk and Lilly	Mounjaro May 2022; the weekly insulins March 26 and September 23, 2026	6, 8
Cancer immunotherapy	Keytruda, and its injection under the skin, Keytruda Qlex	Merck	Keytruda 2014; Qlex September 2025	7
Antibody-drug conjugate	Enhertu	AstraZeneca and Daiichi Sankyo	Approved December 2019	7
Newest cancer pills	Veppanu (vepdegestrant), the first PROTAC-type protein degrader; Rasonque (daraxonrasib), a RAS inhibitor	Arvinas and Pfizer; Revolution Medicines	Approved May 1 and August 26, 2026	7
Cell therapy	Carvykti	Johnson & Johnson and Legend Biotech	Approved February 2022	7
Cholesterol, newest	Lipfendra (enlicitide), the first oral PCSK9 inhibitor	Merck	Approved July 15, 2026	8
Immunology	Dupixent; Skyrizi; Icotyde (icotrokinra), the first oral IL-23 drug	Sanofi and Regeneron; AbbVie; Johnson & Johnson	2017; 2019; March 17, 2026	9
Gene editing	Casgevy, the only approved CRISPR medicine; lonvo-z, the first in-body editor with Phase III results	Vertex and CRISPR Therapeutics; Intellia	Casgevy November 2023 (UK) and December 2023 (US); lonvo-z under FDA priority review, decision due March 10, 2027	10
Gene therapy	Zolgensma, the largest seller; Fayuvi, the newest	Novartis; Ultragenyx	2019; September 2026	10
RNA medicine	Amvuttra (vutrisiran)	Alnylam	Heart indication approved March 2025	10
mRNA	mFLUSIVA, the first mRNA flu vaccine	Moderna	Approved August 5, 2026	11
Alzheimer's disease	Leqembi; Kisunla	Eisai and Biogen; Eli Lilly	Full approval July 2023; July 2024	12
HIV prevention	Yeztugo (lenacapavir), an injection twice a year	Gilead	Approved June 2025; African launches from December 2025	13
AI-discovered drugs	Rentosertib; zasocitinib, designed by computer	Insilico Medicine; Takeda	Phase III since mid-2026; FDA decision due early 2027	15

Category	Leading or newest product	Maker	Approved or status	Module
Protein-structure prediction	AlphaFold 3	Google DeepMind and Isomorphic Labs	Published May 2024	15
Devices	FreeStyle Libre and Dexcom glucose monitors; da Vinci 5 and Hugo surgical robots	Abbott and Dexcom; Intuitive and Medtronic	In service; da Vinci 5 March 2024; Hugo cleared December 2025	18

FDA records, company announcements, and press reports.

Who's Who

The Companies, Agencies, and Other Bodies This Course Names

Name	What it is	Based in
Abbott	Device and diagnostics maker; the FreeStyle Libre glucose monitors	US
AbbVie	Drug maker of Humira, Skyrizi, and Rinvoq	US
Achaogen and Melinta	Antibiotic makers that went bankrupt after winning approval	US
ACIP (Advisory Committee on Immunization Practices)	The CDC's vaccine advisory committee	US
Akeso	Biotech that discovered ivonescimab	China
Alnylam	The leading maker of RNA-interference drugs, including Amvuttra	US
Alphabet and Google DeepMind	Google's parent and its AI laboratory, which built AlphaFold	US; Britain
Alzheimer's Association	Patient and research organization that counts US cases	US
American Academy of Pediatrics	Pediatricians' society that sued over the federal vaccine changes (Module 11)	US
Amgen	Biotech maker of Repatha and MariTide	US
AMR Action Fund	Industry-backed fund that invests in new antibiotics	International
Arrowhead and Esperion	Makers of Redemplo and Nexletol	US
Arvinas	Biotech that developed Veppanu with Pfizer	US
AstraZeneca	Drug maker of Tagrisso, Enhertu (with Daiichi Sankyo), and Farxiga	Britain
BARDA (Biomedical Advanced Research and Development Authority)	The US agency that funds vaccines and other medical countermeasures	US
Bayer and Boehringer Ingelheim	Drug makers of Kerendia and of Jardiance (with Lilly)	Germany
BeOne Medicines	Cancer-drug maker formerly called BeiGene; maker of Beqalzi	Switzerland, founded in China
Biogen	Biotech that made Aduhelm and co-markets Leqembi	US
BioMarin and CSL	Makers of the hemophilia gene therapies Roctavian and Hemgenix	US; Australia
BioNTech	Biotech that developed the Pfizer COVID vaccine	Germany
bluebird bio	Gene-therapy pioneer (Module 10)	US
Boston Scientific	Maker of heart devices such as Watchman and Farapulse	US
Bristol Myers Squibb	Drug maker of Opdivo, Eliquis (with Pfizer), and Cobenfy	US
CDC (Centers for Disease Control and Prevention)	The US public-health agency	US
CEPI (Coalition for Epidemic Preparedness Innovations)	Global fund for vaccines against epidemic threats	International
Children's Hospital of Philadelphia	Hospital that gave the first personalized gene edit	US
CMS (Centers for Medicare & Medicaid Services)	The agency that runs Medicare and Medicaid and negotiates Medicare drug prices	US
Commerce and Defense Departments	US departments that set the drug tariffs and keep the 1260H list of Chinese military companies	US
CRISPR Therapeutics	Biotech that developed Casgevy with Vertex	Switzerland and US

Name	What it is	Based in
CSPC Pharmaceutical, Hengrui, Innovent, RemeGen, and 3SBio	Chinese drug makers that license candidates to Western companies	China
CVC and GBL	Investment firms buying Recordati	Luxembourg; Belgium
Daiichi Sankyo	Drug maker that co-developed Enhertu and Datroway	Japan
DaVita and Fresenius	The largest dialysis companies	US; Germany
Dexcom, Insulet, and Tandem	Makers of glucose monitors and insulin pumps	US
Dr. Reddy's and Hetero	Generic makers that will supply lenacapavir (Module 13)	India
Edwards, Zimmer Biomet, BD, and Smith+Nephew	Makers of heart valves, orthopedic implants, and hospital supplies	US; Britain
Eisai	Drug maker that developed Leqembi	Japan
Eli Lilly	Drug maker of Mounjaro, Zepbound, Foundayo, and Kisunla	US
EMA (European Medicines Agency)	The EU's drug regulator	EU (Amsterdam)
Evaluate, IQVIA, and Citeline	Data firms whose market and pipeline figures the course cites	Britain; US; Britain
Exact Sciences	Maker of the Cologuard screening test, owned by Abbott since March 2026	US
Express Scripts, CVS Caremark, and Optum Rx	The three largest pharmacy benefit managers (PBMs), owned by Cigna, CVS Health, and UnitedHealth	US
FDA (Food and Drug Administration)	The US regulator of drugs, biologics, and devices; its centers are CDER, CBER, and CDRH	US
FTC (Federal Trade Commission)	The US competition regulator that sued the PBMs	US
Fujirebio and Roche Diagnostics	Makers of the first cleared Alzheimer's blood tests	Japan; Switzerland
Gates Foundation	The largest private funder of global health	US
Gavi	The vaccine alliance that buys vaccines for poor countries	International (Geneva)
GE HealthCare, Philips, Siemens Healthineers, and Danaher	Makers of imaging and diagnostic equipment	US; Netherlands; Germany; US
Generate, Absci, Chai, Latent Labs, and Lila	AI drug-design start-ups	US; Britain
Gilead	Drug maker of HIV medicines, including lenacapavir	US
Global Fund	International fund for HIV, tuberculosis, and malaria	International (Geneva)
Grail	Maker of the Galleri multi-cancer blood test	US
GSK	Drug and vaccine maker of Shingrix and bepirovirsen	Britain
Guardant and Foundation Medicine	Makers of liquid-biopsy cancer tests	US
HHS (Department of Health and Human Services)	The US department over the FDA, CDC, NIH, and CMS	US
ICER (Institute for Clinical and Economic Review)	Nonprofit that assesses drugs' value for money	US
ICH (International Council for Harmonisation)	The body that sets common technical standards for drug approval	International
Illumina and MGI	Makers of DNA sequencers	US; China
Insilico Medicine	AI drug-discovery company that developed rentosertib	Hong Kong and US
Intellia	Gene-editing company developing lonvo-z and nex-z	US

Name	What it is	Based in
Intuitive Surgical	Maker of the da Vinci surgical robots	US
Ionis	The leading maker of antisense drugs	US
Isomorphic Labs	Alphabet's AI drug-discovery company	Britain
Johnson & Johnson	Drug and device maker of Stelara, Darzalex, Carvykti (with Legend Biotech), and Icotyde	US
Kailera	Obesity-drug company built on Hengrui's candidates	US
KFF	Health-policy research organization that polls drug use	US
Knoa Pharma	The foundation-owned successor to Purdue Pharma's business	US
Legend Biotech	Cell-therapy company that developed Carvykti with Johnson & Johnson	US, founded in China
Lonza, Samsung Biologics, Fujifilm Diosynth, and Thermo Fisher	The largest contract manufacturers	Switzerland; South Korea; Japan; US
Madrigal	Maker of Rezdiffra for fatty liver disease	US
McKesson, Cardinal Health, and Cencora	The three largest drug wholesalers	US
Medicines for Malaria Venture, TB Alliance, and DNDi	Nonprofits that develop drugs for neglected diseases	Switzerland; US; Switzerland
Medicines Patent Pool	UN-backed body that licenses patents for generic production in poor countries	International (Geneva)
Medtronic and Stryker	The largest pure device makers	US (Medtronic domiciled in Ireland)
Merck & Co.	Drug maker of Keytruda, Gardasil, and Lipfendra (called MSD outside the US and Canada)	US
MHRA, PMDA, and NMPA	The drug regulators of Britain, Japan, and China	Britain; Japan; China
Mindray and United Imaging	Chinese makers of monitors and imaging machines	China
Moderna	Maker of mRNA vaccines, including Spikevax and mFLUSIVA	US
National Security Commission on Emerging Biotechnology	Congressional commission on US biotechnology strategy	US
Neuralink, Synchron, and Precision Neuroscience	Makers of brain-computer interfaces	US
NICE and IQWiG	The bodies that assess drugs' value in England and Germany	Britain; Germany
NIH (National Institutes of Health)	The largest public funder of biomedical research	US
Nimbus Therapeutics and Schrödinger	The developer of zasocitinib and the maker of the design software it used	US
Novartis	Drug maker of Entresto, Kisqali, Pluvicto, Leqvio, and Zolgensma	Switzerland
Novo Nordisk	Drug maker of Ozempic, Wegovy, and the insulins	Denmark
Nuvalent	Biotech that developed Jideytro, bought by GSK	US
Nvidia, Microsoft, and Amazon	Technology companies that supply computing for drug discovery	US
OMB (Office of Management and Budget)	White House office that will list biotech companies of concern	US
Pan American Health Organization	The WHO's office for the Americas	International (Washington)

Name	What it is	Based in
PEPFAR	The US program for HIV in poor countries	US
Pfizer	Drug maker of Prevnar, Comirnaty (with BioNTech), and Ibrance	US
PharmCube and PitchBook	Data firms that count licensing and acquisition deals	China; US
Protagonist	Biotech that developed Icotyde with Johnson & Johnson	US
PTC Therapeutics, Rocket Pharmaceuticals, and Ultragenyx	Makers of gene therapies for ultra-rare diseases	US
Purdue Pharma	Maker of OxyContin (Module 16)	US
RAND	Research organization that compares drug prices across countries	US
Recursion	AI drug-discovery company, merged with Exscientia	US
Regeneron	Biotech that developed Dupixent with Sanofi	US
Revolution Medicines	Biotech that developed Rasonque	US
Roche	Drug and diagnostics maker; owner of Spark Therapeutics	Switzerland
Sandoz, Teva, Viatris, Celltrion, and Samsung Bioepis	The largest generic and biosimilar makers	Switzerland; Israel; US; South Korea; South Korea
Sanofi	Drug and vaccine maker of Dupixent (with Regeneron) and Beyfortus (with AstraZeneca)	France
Sarepta	Maker of the Duchenne gene therapy Elevidys	US
Serum Institute of India	The world's largest vaccine maker by doses; maker of the R21 malaria vaccine	India
Summit Therapeutics	Biotech that holds ivonescimab outside China	US
Sun Pharma	Generic and specialty maker buying Organon	India
Supernus	Owner of Zurzuvae after buying Sage	US
Takeda	Drug maker of zasocitinib and Orzeyful	Japan
Theranos	Blood-testing company that collapsed in fraud	US
Unitaid and UNICEF	Agencies that buy and fund medicines and vaccines for poor countries	International
USAID	The US foreign-aid agency (Module 13)	US
Vanda, Otsuka, and Vera Therapeutics	Makers of Bysanti, Simtriyo, and Trutakna	US; Japan; US
Vertex	Drug maker of Casgevy (with CRISPR Therapeutics) and Journavx	US
Verve	Gene-editing company bought by Lilly	US
WHO (World Health Organization)	The UN's health agency	International (Geneva)
WuXi AppTec and WuXi Biologics	Contract research and manufacturing companies serving Western biotech	China
Xaira Therapeutics	AI protein-design company	US

Organizations grouped in one row share a role. Figures and dates are in the modules.

Module 1 — Foundations

What a Drug Is

Recommended Reading / Reference

Book: Siddhartha Mukherjee, *The Gene: An Intimate History*

Reference: IQVIA Institute, *Global Use of Medicines* (annual); Evaluate, *World Preview* (annual)

1a. Small Molecules and Biologics

Medicines come in two families. Small molecules, such as aspirin, statins, and most pills, are chemicals of a few dozen atoms. They are made by synthesis in a factory, cheap to produce, stable on a shelf, and able to enter cells, and they were the whole of pharmacy until the 1980s and remain most prescriptions. Biologics are large molecules made by living cells, such as proteins, antibodies, and hormones. They contain thousands of atoms, must usually be injected, and cost far more to make, but they can do things small molecules cannot: bind one target with great precision, replace a missing protein, or recruit the immune system. Recombinant insulin and the monoclonal antibodies that followed built the modern industry, and biologics now account for most of the top-selling drugs and most of the cost.

1b. The Modalities

Modality	What it is	First approved	Examples	Cost to make a dose
Small molecule	A synthesized chemical, usually a pill	1899 (aspirin)	Eliquis, Paxlovid, imatinib, orforglipron	Cents to dollars
Peptide	A short chain of amino acids, injected or now taken as a pill	1922 (insulin); recombinant 1982	Semaglutide, tirzepatide, the insulins	Dollars
Monoclonal antibody	An engineered immune protein that binds one target	1986 (muromonab)	Keytruda, Dupixent, Skyrizi, Humira	$50-500
Antibody-drug conjugate (ADC)	An antibody that carries a toxic payload to a tumor	2000 (Mylotarg)	Enhertu, Padcev, Trodelvy	Hundreds of dollars
Bispecific antibody	An antibody that binds two targets	2009 (EU, Removab); 2014 (US, Blincyto)	Tecvayli, Columvi, ivonescimab (China)	Hundreds of dollars
Targeted protein degrader	A molecule that tags a disease protein for the cell to destroy	The newest modality (State of the Art)	Vepdegestrant	Dollars
mRNA	Messenger RNA that instructs cells to make a protein	2020 (COVID vaccines)	Comirnaty, Spikevax, Moderna's flu vaccine	Dollars
RNA interference and antisense	Short RNA strands that silence a gene	1998 (fomivirsen); 2018 (Onpattro)	Amvuttra, Leqvio, Spinraza	Hundreds to thousands of dollars
Gene therapy	A virus that delivers a working gene	2012 (EU); 2017 (US)	Zolgensma, Hemgenix, Elevidys	Hundreds of thousands of dollars, once
Gene editing	CRISPR or a related tool that corrects the gene itself	Casgevy (State of the Art)	Casgevy; the first personalized edit (Module 10)	Hundreds of thousands of dollars, once

Modality	What it is	First approved	Examples	Cost to make a dose
Cell therapy	Engineered immune cells (CAR-T) or donor cells	By 2010 (Provenge); CAR-T 2017 (Kymriah)	Yescarta, Carvykti, Breyanzi	Hundreds of thousands of dollars
Radiopharmaceutical	A radioactive atom attached to a targeting molecule	By 2002 (Zevalin); Lutathera 2018	Pluvicto	Thousands of dollars
Vaccine	Weakened, inactivated, or partial forms of a germ that train immunity	1796 (smallpox)	Prevnar, Gardasil, Shingrix	Dollars

Costs are rough orders of magnitude; sales figures are in the modules on each therapeutic area.

1c. How Drugs Work

A drug acts on a target, usually a protein such as a receptor on a cell's surface, an enzyme, or an ion channel. It blocks the target (an antagonist or inhibitor), activates it (an agonist), or, in the newer modalities, destroys it or replaces or silences the gene that makes it. Statins inhibit an enzyme that makes cholesterol, the GLP-1 drugs activate a hormone receptor, Keytruda blocks a protein that switches off immune cells, and Casgevy edits a gene that suppresses fetal hemoglobin. Drug discovery is the search for a target whose modulation changes a disease, and for a molecule that modulates it without touching the thousands of other proteins that look similar. The industry's central lesson, learned over a century, is that most targets that look promising in a test tube do nothing in a person, which is why so few drugs that enter human trials succeed (Module 2). Human genetics, which shows what a target does when nature mutates it, has become the best guide: a 2024 analysis by Eric Minikel and colleagues found that drugs whose targets have genetic support are more than twice as likely to reach approval.

1d. The Scale

	Figure	Note
Global spending on medicines	About $1.6 trillion a year	Nearly half in the United States, which has 4% of the world's people
US spending	About $700 billion at list prices; about $500 billion after rebates	Roughly a tenth of US health spending
Industry research and development	About $300 billion a year	About 20% of revenue at the largest companies
New drugs approved by the FDA	About 50 a year through the 2020s	The counts by year in Module 2
Companies	About a dozen giants (Module 3) and about 5,000 biotechs	Most biotechs have no product on sale
Largest company by market value	Eli Lilly (Module 3)	On its obesity drugs (Module 6)
Largest drug	Tirzepatide (Mounjaro and Zepbound)	Sales in Module 6

Approximate; IQVIA and FDA figures; market value as of October 2026.

Module 1 Key Points

Foundations

• Medicines are small molecules, cheap chemicals that enter cells, or biologics, large proteins grown in living cells that dominate the top sellers.

• Newer modalities, from antibody-drug conjugates and mRNA to gene editing and protein degraders, each attack disease at a different step.

• A drug blocks, activates, destroys, replaces, or silences a target, and most targets that look promising fail in people.

• Targets backed by human genetics are more than twice as likely to yield an approved drug.

• The world spends about $1.6 trillion a year on medicines, nearly half of it in the United States.

Module 1 Quiz

Check Your Understanding

1. What separates a biologic from a small molecule?

A) Biologics are pills
B) Small molecules are grown in living cells and injected
C) Only biologics need FDA approval
D) Biologics are large proteins made by living cells, usually injected, and costlier to make

2. What does a targeted protein degrader do?

A) Blocks a receptor on the cell surface, as most antibodies do
B) Tags a target protein for destruction
C) Edits the gene
D) Delivers a toxic payload to a tumor cell, like an antibody-drug conjugate

3. Why do most drugs that enter human trials fail?

A) Trials are too small
B) Regulators reject drugs for being too expensive to manufacture at scale, even when they work
C) Targets that look promising in the lab do nothing in people
D) Patients stop taking them

4. What does human genetic support do for a drug target?

A) It more than doubles the odds of approval.
B) It guarantees that the drug will reach the market.
C) It makes the drug cheaper to manufacture at large scale.
D) It allows the company to skip the first phase of human trials.

5. Roughly how much does the world spend on medicines a year?

A) About $500 billion, mostly in Europe
B) About $10 trillion, a third of it in China after its reimbursement reforms
C) About $160 billion a year
D) About $1.6 trillion

Module 2 — From Lab to Market

Discovery, Trials, and Approval, With the Numbers

Recommended Reading / Reference

Reference: FDA, *The Drug Development Process*; DiMasi and colleagues (2016) and Wouters and colleagues (2020) on research costs; BIO, Informa, and QLS, *Clinical Development Success Rates 2011-2020* (2021); the FDA's guidance on expedited programs

2a. Discovery and Preclinical Work

A drug begins with a target and a hypothesis, that blocking this protein will slow this disease, drawn from genetics, biology, or increasingly from population studies that link a gene variant to a condition. Chemists or biologists then find a molecule that hits the target, by screening millions of compounds, designing one from the target's structure, or engineering an antibody. The candidate is optimized for potency, selectivity, and survival in the body, and tested in cells and animals for toxicity. Three to six years and tens of millions of dollars produce a candidate that may enter human trials.

2b. The Phases

Phase	Participants	Purpose	Duration	Typical cost	Share that advance (2011-20)	Main cause of failure
Preclinical	Cells and animals	Toxicity, dose, and mechanism	1-2 years	$5-20M	Most never reach people	Toxicity; no effect
Phase I	20-100 healthy volunteers (patients, in cancer)	Safety and dose	About 1 year	$5-15M	52%	Toxicity
Phase II	100-500 patients	A first sign of efficacy; choosing the dose	About 2 years	$20-60M	29%, the graveyard	The biology was wrong
Phase III	300 to several thousand patients, randomized and usually blinded	Confirming benefit and safety against placebo or standard care	3-4 years	$100-500M, up to $1B in heart disease	58%	Too small an effect; safety; commercial
Review	—	Assessment by the FDA or Europe's EMA	6-12 months	A user fee of about $4.7M	91%	Manufacturing ; data quality
Phase IV	Patients in routine care	Long-term safety; new uses	Ongoing	Varies	—	Rare side effects surface
Overall			10-15 years	$1-3B per approved drug, counting failures and capital	7.9% from Phase I (6.7% in 2014-23 data)	Lowest in urology (3.6%) and cancer (about 5%); highest in hematology (24%)

BIO, Informa, and QLS (2021); Citeline for 2014-23; academic cost estimates. Rates vary widely by disease.

Phase II is where most drugs die, because it is where a hypothesis first meets a patient, and Phase III is where failure is most expensive. The cost of a new drug, including the failures it must pay for and the capital tied up for a decade, is the figure the industry cites to justify its prices and its critics contest: academic estimates run from under $1 billion for small companies to over $4 billion for the largest ones.

2c. The Fast Lanes

Pathway	Criterion	What it gives	Note
Standard review	Any drug	A review of about ten months	The default
Priority review	A significant improvement over existing treatment	A review of about six months	About half of novel approvals
Fast track	A serious condition with unmet need	Rolling submission and more FDA meetings	—
Breakthrough therapy	Early evidence of substantial improvement	Intensive FDA guidance, often with priority review	A large share of approvals since 2012
Accelerated approval	A serious condition and a surrogate endpoint 'reasonably likely' to predict benefit	Approval before confirmatory trials finish	The workhorse of cancer approvals, and the Aduhelm dispute (Module 12)
Priority review voucher	Approval of a drug for a rare pediatric or tropical disease, or a medical countermeasure	A tradeable voucher for a six-month review of a later drug	Recent sales near $150 million
Commissioner's National Priority Voucher	Chosen by the FDA commissioner for national priorities, such as affordability or US manufacturing	A target review of one to two months	A 2025 pilot; seven drugs approved under it by May 2026, among them Lilly's obesity pill after 50 days
Emergency use authorization	A declared emergency	Use before full approval	The COVID vaccines and antivirals
Orphan designation	A disease with fewer than 200,000 US patients	Exclusivity (Module 5), tax credits, and fee waivers	About half of novel approvals

The FDA's drug center approved 50 novel drugs in 2024 and 46 in 2025, a decline during the agency's turmoil (Module 16), and 45 by September 28, 2026, the fastest pace in years. The pandemic's emergency authorizations showed what a year could do when everything was prioritized (Module 11).

2d. After Approval

Approval is where the money starts. A drug is sold under patents and regulatory exclusivity (Module 5), priced to recover its cost and its failures, and promoted to physicians and, in the United States and New Zealand alone, to consumers on television. It gathers new indications through further trials, which extend its life and revenue; Keytruda has more than 40. Its safety is tracked after launch, and withdrawals such as Vioxx's are rare and catastrophic (Module 16). At the end it faces the cliff of Module 5, the day generics or biosimilars arrive.

Module 2 Key Points

From Lab to Market

• Discovery and animal testing take three to six years and tens of millions of dollars, and most candidates never reach people.

• Only about 8% of drugs entering human trials reach approval; Phase II, where the biology is first tested, is the graveyard.

• A new drug takes 10-15 years and $1-3 billion, counting the failures and the capital tied up.

• Fast lanes include priority review, breakthrough status, accelerated approval, and since 2025 the commissioner's one-to-two-month vouchers.

• The FDA approved 46 novel drugs in 2025, down from 50, and 45 by late September 2026.

Module 2 Quiz

Check Your Understanding

1. In which phase do most drugs fail?

A) Phase I
B) Phase II, the graveyard
C) Phase III
D) Review

2. What share of drugs entering human trials won approval in the 2011-20 data?

A) About 1%
B) About a quarter, with cancer drugs the most likely to succeed
C) About 8%, or roughly one in twelve
D) About half

3. What did Lilly's obesity pill use to win a 50-day review?

A) A national priority voucher
B) Breakthrough status
C) A rare pediatric disease voucher bought from another company for about $150 million in 2025
D) An emergency use authorization

4. What does accelerated approval allow?

A) It lets any drug skip Phase I.
B) It allows approval on a surrogate endpoint, with confirmation later.
C) It guarantees a six-month review for every drug that treats a rare disease.
D) It exempts cancer drugs from the requirement for randomized trials of any kind.

5. How did the FDA's count of novel approvals change in 2025?

A) It fell to 46 from 50.
B) It rose to a record 55 approvals.
C) It held steady at about 50 for the year.
D) It collapsed to about 20 after the staff cuts.

Module 3 — The Industry

Big Pharma and Biotech

Recommended Reading / Reference

Reference: Evaluate, *World Preview* (annual); company annual reports; BioPharma Dive and Fierce Biotech; PitchBook's biopharma reports

3a. Big Pharma

Company	Home	Revenue (2025)	Top drugs	Largest cliff ahead	Position (October 2026)
Eli Lilly	US	$65.2B; 2026 guidance $85-87B	Mounjaro, Zepbound, Foundayo, Verzenio, Kisunla	None major before the 2030s	The obesity winner and the most valuable drugmaker
Novo Nordisk	Denmark	About $46B; 2026 guidance a decline of up to 6%	Ozempic, Wegovy (injection and pill), insulins	Semaglutide (Modules 5 and 6)	Lost the lead; restructuring
Johnson & Johnson	US	About $94B, including devices	Darzalex, Tremfya, Stelara, Rybrevant, Carvykti	Stelara, now	Diversified across drugs and devices
Merck	US	About $65B	Keytruda, Gardasil, Winrevair	Keytruda, the largest single cliff (Module 5)	Buying to fill the gap: Verona, Cidara, Terns
AbbVie	US	About $61B	Skyrizi, Rinvoq, Botox	Humira's, already absorbed (Module 9)	The model of surviving a cliff; bought Apogee (Module 5)
Pfizer	US	About $62B	Eliquis, Vyndaqel, Prevnar, Padcev	Eliquis and Ibrance	Post-COVID contraction; the Metsera obesity bet
AstraZeneca	UK	About $59B	Tagrisso, Imfinzi, Enhertu, Farxiga	Farxiga	The oncology leader; the largest licensing bets in China (Module 14)
Roche	Switzerland	About CHF 61B, or $74B	Ocrevus, Hemlibra, Vabysmo; diagnostics	Biosimilars, largely absorbed	Drugs and diagnostics together
Novartis	Switzerland	About $55B	Entresto, Cosentyx, Kisqali, Pluvicto, Leqvio	Entresto (Module 5)	Pure pharma after spinning off Sandoz; bought Avidity
Bristol Myers Squibb	US	About $48B	Eliquis (with Pfizer), Opdivo, Cobenfy	Eliquis and Opdivo (Module 5)	The deepest cliff relative to its size

Company	Home	Revenue (2025)	Top drugs	Largest cliff ahead	Position (October 2026)
GSK	UK	About £33B, or $43B	Shingrix, Arexvy, HIV drugs, Nucala	Dolutegravir, 2028-29	Vaccines and infectious disease; bought Nuvalent (Module 5)
Sanofi	France	About €44B, or $49B	Dupixent, vaccines, Beyfortus	Dupixent (Module 5)	Immunology
Amgen	US	About $36B	Repatha, Tezspire, Enbrel; MariTide (Module 6)	Enbrel, eroding	An obesity contender
Gilead, Regeneron, Vertex, Takeda, Bayer, Boehringer Ingelheim (private)	US, Japan, Germany	$12-50B each	HIV drugs and lenacapavir; Dupixent and Eylea; cystic fibrosis and Casgevy; Entyvio; Xarelto; Jardiance	Eylea now; Xarelto	Specialists

Approximate, from company reports; revenue converted at 2025 exchange rates where needed.

About a dozen companies with revenues of $40-100 billion each dominate the industry. Their model is to develop some drugs internally, license or acquire most of their pipelines from biotechs, run the global trials and regulatory filings that biotechs cannot afford, manufacture at scale, and market through sales forces of thousands. They are increasingly the industry's buyers and integrators rather than its inventors, since most new drugs originate outside them. The ranking in October 2026 shows the industry's stories at once. Lilly passed $1 trillion in market value in 2025 and is worth about $1.1 trillion on its obesity drugs, while Novo, worth about $600 billion at its 2024 peak, is worth about $175 billion on the same class of drugs. Merck, Bristol, and Pfizer meanwhile face the loss of their largest products (Module 5).

3b. Biotech and Its Cycle

Year	Biotech IPOs	Context
2021	About 100 worldwide, a record	The boom: hundreds of companies listed at inflated values
2022	Just over 20	The bust: the IPO window shut
2023-24	Few	Survivors traded below their cash; layoffs and mergers
2025	8 in the US, the fewest in at least five years	Licensing to Big Pharma, much of it of Chinese drugs, became the main exit (Module 14)
2026, to September	10 in the first quarter alone; Kailera's April listing raised about $719 million, the largest US biotech IPO since 2021	The reopening

Labiotech and Life Science Daily counts; Kailera's figure includes the over-allotment.

Several thousand biotechnology companies do the inventing, concentrated in Boston and Cambridge, the San Francisco Bay Area, San Diego, and now Shanghai and Suzhou. Most have one or two programs, no revenue, and a decade to burn through venture capital and public-market money before an approval or an acquisition. The financing cycle is brutal, as the table shows, and the biotech index has historically moved with interest rates as much as with science, because a company with no revenue for a decade is a long-duration asset. The 2026 reopening came as rates eased, acquisitions accelerated (Module 5), and investors bet that the pricing fights of Module 17 would spare the drugs that work.

3c. The Geography

The industry has three centers. The United States is the largest market, the largest source of revenue and profit, the home of most of Big Pharma and most biotech, and the regulator whose approval matters most. Europe, chiefly Switzerland, Britain, Denmark, Germany, and France, is the home of half of Big Pharma and a market that pays far less than the American price (Module 17). China is the new third: a leading source of new drug candidates, the fastest trials, and a licensing partner to every Western company (Module 14). Manufacturing is spread across Ireland, for its tax rates, Singapore, India, and China, and it is the target of the US tariffs in Module 17.

Module 3 Key Points

The Industry

• About a dozen companies with $40-100 billion of revenue dominate; Lilly, at about $1 trillion, is the most valuable.

• Novo fell from about $600 billion to about $175 billion on the same class of drugs that lifted Lilly.

• Big Pharma increasingly buys or licenses its pipeline; most new drugs originate in biotechs.

• Biotech IPOs fell to eight in the US in 2025 and reopened in 2026, led by Kailera's $719 million listing.

• The industry has three centers: the United States, Europe, and China.

Module 3 Quiz

Check Your Understanding

1. What happened to Novo Nordisk's market value?

A) It doubled on the Wegovy pill.
B) It passed Lilly's for the first time.
C) It fell from about $600 billion to about $175 billion.
D) It stayed near its peak of $600 billion as sales of Ozempic grew.

2. Which company is the most valuable drugmaker?

A) Novo Nordisk
B) Merck
C) AbbVie
D) Eli Lilly, near $1 trillion

3. Where do most new drugs originate?

A) Big Pharma's labs
B) Universities and government institutes, which by law must hand their discoveries to the largest companies
C) In biotech companies
D) At the FDA

4. How many US biotech IPOs were there in 2025?

A) About 110
B) About 30, a reopening year
C) About 75
D) Eight, the fewest in at least five years, before a 2026 reopening

5. Which three centers does the industry have?

A) The US, Japan, and Brazil
B) US, Europe, China
C) Europe, India, and Russia, where most active ingredients are made
D) The United States and Japan only

Module 4 — The Chain Beneath

Manufacturers, Generics, and Middlemen

Recommended Reading / Reference

Reference: The Association for Accessible Medicines' annual generic-savings report; the FTC's reports and settlements on pharmacy benefit managers (2024-26); IQVIA on biosimilars; Drug Channels on the gross-to-net bubble

4a. Contract Manufacturers

Company	Home	Revenue (2025, approx.)	What it makes	Note
Lonza	Switzerland	About $7B	Biologics, cell and gene therapies, small molecules	The largest Western contract maker
Samsung Biologics	South Korea	About $3B	Antibodies, at the world's largest single site (Songdo)	—
WuXi AppTec and WuXi Biologics	China	About $6B and $3B	Small-molecule development and manufacturing; biologics	Targets of the BIOSECURE Act (below)
Catalent	US (owned by Novo Holdings)	About $4B	Filling and finishing; gene therapy; GLP-1 capacity	Bought to secure Wegovy supply (Module 5)
Thermo Fisher (Patheon), Fujifilm Diosynth, Boehringer Ingelheim, Charles River	US, Japan, Germany	$2-8B each	Full service; biologics; preclinical testing	—
Syngene, Divi's, Piramal	India	$0.5-1B each	Small molecules	—

Approximate, from company reports.

Contract development and manufacturing organizations (CDMOs) make drugs for companies that do not own plants, which means most biotechs and, increasingly, Big Pharma for biologics. The US BIOSECURE Act, debated since 2024, became law on December 18, 2025, inside the annual defense bill. It names no companies. Instead, a 'biotechnology company of concern' is one on the Pentagon's list of Chinese military companies, known as the 1260H list, that the budget office finds is involved in biotech, or one the budget office designates directly; that list is due by December 18, 2026. Federal agencies and their contractors will then be barred from new work with listed firms once procurement rules are revised, around 2028, while existing contracts keep five more years of protection. WuXi AppTec was added to the 1260H list in June 2026. The debate had already moved sourcing: Western clients shifted programs to Samsung, Lonza, and Indian makers, and WuXi AppTec sold its US and British cell and gene therapy unit in 2025. Manufacturing is also where the tariffs of Module 17 bite, since about half of America's branded drugs by value are made abroad, in places such as Ireland, Switzerland, and Singapore.

4b. Generics and Biosimilars

Segment	Share of US prescriptions	Share of US spending	Leaders	Economics
Small-molecule generics	About 90%	About 13%	Teva, Sandoz, Viatris, Sun, Dr. Reddy's, Cipla, Lupin	Prices fall 80-90% within a year of entry; thin margins
Biosimilars	A few percent, rising	A few percent	Sandoz, Amgen, Samsung Bioepis, Celltrion, Biocon	Discounts of 30-80%; slower erosion than generics
Branded drugs	About 10%	Most of the rest	Big Pharma	Monopoly pricing during exclusivity

Association for Accessible Medicines and IQVIA; approximate.

Generics are the most effective cost control in American medicine, saving $467 billion in 2024 by their makers' count, and their economics mirror those of branded drugs: a race to the bottom that produces shortages of sterile injectables, chemotherapy drugs, and ADHD medicines when prices fall below the cost of quality production. India supplies about 40% of American generics by volume and relies on China for most of their active ingredients, which makes the cheapest drugs the most exposed to geopolitics. Biosimilars, the copies of biologics, are harder to make. Humira's US sales fell by about two-thirds in the two years after its biosimilars arrived, and the wave led by Stelara, Eylea, and Prolia (Module 5) is testing whether the US market, where formularies decide, adopts them as fast as Europe did.

4c. The Middlemen

Layer	Companies	Concentration	What they do	Issue in 2026
Pharmacy benefit managers (PBMs)	CVS Caremark, Express Scripts (Cigna), Optum Rx (UnitedHealth)	About 80% of US prescriptions	Negotiate rebates from manufacturers for insurers, set formularies, and own mail-order and specialty pharmacies	The FTC's insulin case and the February 2026 reform law (below)
Wholesale distributors	McKesson, Cencora, Cardinal Health	About 90% of US drug distribution	Move nearly every pill from manufacturer to pharmacy on margins of 1-2%	Their share of the opioid settlements (Module 16)
Pharmacies	CVS, Walgreens, Walmart, Kroger, independents, specialty pharmacies	Chains about 60%	Dispense; specialty pharmacies handle biologics	Walgreens taken private in 2025; independents closing
Insurers	UnitedHealth, Elevance, CVS-Aetna, Cigna, Humana; Medicare and Medicaid	Top five about half of commercial coverage	Pay, with cost-sharing designs that decide what patients see	Scrutiny of Medicare Advantage; UnitedHealth's 2025 crisis
Group purchasing organizations	Vizient, Premier	About 90% of hospital purchasing	Negotiate hospitals' drug and supply contracts	—

The middlemen are where the American system's peculiarity lives. A drug's list price is not what anyone pays. The manufacturer pays rebates to the PBM in exchange for a place on its formulary, worth hundreds of billions of dollars a year across the industry, and the PBM passes some to the insurer and keeps some. The patient's cost-sharing is often calculated on the list price rather than the net, and the three largest PBMs, each owned by a company that also owns an insurer and a pharmacy, handle most prescriptions (table). The reckoning came in 2026. The FTC's case that PBMs inflated insulin costs was settled by

Express Scripts in February and Caremark in July, with formularies that stop favoring high-list-price versions, cost-sharing based on net prices, and rebates passed through at the counter. The FTC estimates that Caremark's terms alone could save consumers up to $8.5 billion over a decade, and Optum Rx reached a tentative settlement in June 2026, pending the FTC's approval. A law of February 3, 2026, delinks PBMs' pay in Medicare from list prices from 2028 and requires them to pass all rebates to employer plans from 2028-29, though it left out a ban on spread pricing in Medicaid and any structural separation of PBMs from insurers.

4d. Where the Drug Dollar Goes

Worked example — A Branded Drug Listed at $1,000

Follow the money for a branded biologic listed at $1,000 a month. The manufacturer pays a $350 rebate to the PBM for a preferred place on its formulary and gives up $50 in discounts and margins to the wholesaler and pharmacy, netting $600. The PBM passes $300 of the rebate to the insurer and keeps $50 as fees and spread, while the wholesaler earns $15 and the pharmacy $35. The patient's coinsurance is 20% of the $1,000 list price, or $200, so the patient pays a fifth of a price nobody else pays. The insurer pays the remaining $800 and gets $300 back, a net of $500. Together patient and insurer pay $700: the manufacturer's $600 plus the $100 the chain keeps. The more of the price is rebated, the less the insurer pays and the more the patient's share is inflated, which is why PBMs and insurers have favored high-list, high-rebate drugs over cheaper ones. Net-price cost-sharing and PBM pay delinked from list prices, the 2026 reforms, attack exactly this arithmetic.

Module 4 Key Points

The Chain Beneath

• Contract manufacturers make biologics for most biotechs; the BIOSECURE Act, law since December 2025, will bar federal work with listed Chinese firms.

• Generics fill about 90% of US prescriptions for about 13% of spending, but their price wars cause shortages.

• Three PBMs, each owned alongside an insurer and a pharmacy, handle about 80% of US prescriptions.

• Coinsurance on list prices means patients pay a share of a price nobody else pays.

• A February 2026 law delinks Medicare PBM pay from list prices from 2028; the FTC's insulin case is mostly settled.

Module 4 Quiz

Check Your Understanding

1. What is the status of the BIOSECURE Act?

A) Law since December 2025
B) Pending in Congress since 2024, with the WuXi companies named in the text as its targets
C) Vetoed
D) Struck down by a federal court in 2026

2. What share of US prescriptions do generics fill?

A) Half
B) About a quarter, because insurers prefer branded drugs with large rebates to cheap generics
C) About 90%
D) About 60%, rising

3. Who handles about 80% of US prescriptions?

A) Three pharmacy benefit managers
B) Hospitals
C) The federal government, which has negotiated all prices for Medicare and Medicaid since the 2022 law
D) The wholesalers

4. In the worked example, why does the patient pay $200?

A) A tariff
B) Coinsurance is set at 20% of the $1,000 list price, which nobody else pays
C) The pharmacy adds its own markup at the counter
D) The PBM's fee

5. What does the February 2026 PBM law do in Medicare?

A) It splits the PBMs from the insurers that own them.
B) It bans spread pricing in Medicaid from 2027.
C) It caps every drug's list price at its European level.
D) It delinks PBM pay from list prices.

Module 5 — The Patent Cliff and the Business Model

The Economics That Drive Everything Else

Recommended Reading / Reference

Reference: Evaluate's loss-of-exclusivity analyses; IQVIA on biosimilar erosion; PitchBook and EY on biopharma deals; I-MAK's analyses of Humira's patents; the Hatch-Waxman Act and the Biologics Price Competition and Innovation Act

5a. Exclusivity and the Blockbuster

A drug is protected by patents, which last 20 years from filing and leave 10-14 after approval, and by regulatory exclusivity: 5 years for a new chemical entity, 12 for a biologic, and 7 for an orphan drug, with extensions for pediatric studies. During that window it can charge what the market will bear, and in the United States the market has few constraints. A blockbuster, a drug selling over $1 billion a year, pays for the failures, the top hundred drugs earn about half of industry revenue, and a company's fortune rises and falls with a handful of them. The cliff is the day exclusivity ends and copies arrive at steep discounts: generics of small molecules quickly, and biosimilars of biologics more slowly (Module 4).

5b. The Cliff Ahead

Drug	Company	Type	US loss of exclusivity	Company's response
Humira	AbbVie	Biologic	Done (below)	Skyrizi and Rinvoq replaced it (Module 9)
Stelara	Johnson & Johnson	Biologic	2025	Tremfya, Rybrevant, Carvykti
Eylea	Regeneron and Bayer	Biologic	2025-26	High-dose Eylea; Dupixent
Entresto	Novartis	Small molecule	2025	Kisqali, Pluvicto, Leqvio
Prolia and Xgeva	Amgen	Biologic	2025	The obesity pipeline
Ibrance	Pfizer	Small molecule	March 2027	Padcev; the Metsera obesity drugs
Eliquis	Bristol Myers Squibb and Pfizer	Small molecule	April 2028, by settlement	Cobenfy, Camzyos; Medicare's negotiated price (Module 17)
Keytruda	Merck	Biologic	December 2028, when the compound patent expires	Keytruda Qlex (Module 7) and acquisitions
Opdivo	Bristol Myers Squibb	Biologic	2028	A form injected under the skin
Darzalex	Johnson & Johnson	Biologic	2029	Its form injected under the skin
Dupixent	Sanofi and Regeneron	Biologic	About 2031	Still growing (Module 9)
Semaglutide (Ozempic, Wegovy)	Novo Nordisk	Peptide	2032; earlier abroad (Module 6)	The Wegovy pill and CagriSema (Module 6)

Company filings and Labiotech's cliff tracker (2026); dates are the expected first US generic or biosimilar entry.

The industry faces the largest cliff in its history, with roughly $300 billion of annual sales losing exclusivity by the early 2030s; estimates vary with the window chosen. Humira is the template for both the cliff and the response. Its main patent expired in 2016, but AbbVie filed about 250 patent applications on formulations, manufacturing, and dosing, and settled its lawsuits with biosimilar makers on a 2023 US entry date. Biosimilars reached Europe in 2018, while in the United States AbbVie sold more than $100 billion of Humira between 2016 and 2022. The patent system, not the science, set the date. When the cliff came (Module 4), AbbVie had already moved its patients to two successors (Module 9). Merck's response to Keytruda's cliff, an injection under the skin with patents of its own and some $26 billion of acquisitions since 2025, is the current test of whether the template can be repeated at a larger scale.

5c. The Deal Wave

Year	Largest acquisitions	Context
2019	BMS-Celgene $74B; AbbVie-Allergan $63B	The pre-cliff mega-mergers
2020	AstraZeneca-Alexion $39B	A pandemic pause
2021	Merck-Acceleron $11B	Biotech valuations too high to buy
2022	Amgen-Horizon $28B	The biotech bust begins
2023	Pfizer-Seagen $43B; Merck-Prometheus $11B	Antitrust scrutiny of large deals
2024	Novo Holdings-Catalent $16.5B; Vertex-Alpine $5B	China's licensing boom begins (Module 14)
2025	J&J-Intra-Cellular $15B; Novartis-Avidity about $12B; Merck-Verona $10B; Pfizer-Metsera $10B; Merck-Cidara $9.2B; Sanofi-Blueprint $9B	A record licensing year, led by China
2026, to September	Sun Pharma-Organon $11.75B; AbbVie-Apogee $10.9B; GSK-Nuvalent $10.6B; Lilly-Centessa and Gilead-Arcellx $7.8B each; Merck-Terns $6.7B	$106 billion of biopharma takeovers by early June (PitchBook), on pace for more than $250 billion

Announced values; press reports and PitchBook.

The cliff forces the deals. Big Pharma buys biotechs and licenses drugs from them, increasingly from China (Module 14), to fill pipelines that its own laboratories cannot. The shape has changed from the mega-mergers of 2019 to many acquisitions of $5-15 billion, plus licensing deals whose headline values run to billions while their upfront payments are a small fraction.

Worked example — A Licensing Deal From Both Sides

A Chinese biotech has a bispecific antibody in Phase II with a promising signal. A Western company licenses the rights outside China for $300 million upfront, up to $2.7 billion in milestones, and royalties of 10-15% on sales, a '$3 billion deal' in the headline. For the biotech, the $300 million funds five years of work, it keeps China, and the milestones are worth far less than their face value because most drugs fail and the payments come late. For the buyer, assume a one-in-five chance that the drug reaches the market, which is better than Module 2's odds from Phase II because the mechanism is validated. Assume also Phase III costs of about $360 million, sales peaking at $3 billion a year, an operating margin of 50% before a 12.5% royalty, and a 9% discount rate. The deal is then worth about minus $190 million. It pays only if the odds approach one in three, or if the drug becomes a $5 billion blockbuster, in which case it is worth about $400 million at one-in-five odds. The same asset bought from a Western biotech for $1 billion upfront would lose money in all but the best case. That is the 'China discount' at work: the buyer pays less up front, sees Chinese Phase II data sooner, and fills a gap in its cliff years. The loser is the Western biotech that would have charged three times as much for a similar molecule, which is the root of the threat-or-solution debate in Module 14.

Module 5 Key Points

The Patent Cliff and the Business Model

• Patents and regulatory exclusivity give a new drug 10-14 years of protected pricing; biologics get 12 years of data exclusivity.

• About $300 billion of annual sales lose exclusivity by the early 2030s, led by Eliquis, Keytruda, and Opdivo in 2028.

• Humira's patent thicket delayed US biosimilars from 2016 to 2023; Skyrizi and Rinvoq then replaced it.

• The cliff drives the deals: biopharma takeovers reached $106 billion by early June 2026, on pace for more than $250 billion.

• A licensing deal's headline value far exceeds its expected value, which turns on the odds of success and peak sales.

Module 5 Quiz

Check Your Understanding

1. When does Keytruda's US compound patent expire?

A) December 2028
B) 2026
C) March 2027
D) In 2031

2. Why did Humira's US biosimilars arrive only in 2023?

A) Its biosimilars failed FDA review.
B) No company could copy the molecule.
C) AbbVie's patent thicket and settlements delayed entry.
D) Medicare's negotiation program blocked generic versions until its price was set.

3. What does the patent cliff force Big Pharma to do?

A) It forces companies to cut prices on all their other drugs at once.
B) It forces them to merge with generic makers.
C) It forces them to stop research for several years.
D) It forces them to buy pipelines.

4. What did PitchBook count in biopharma takeovers by early June 2026?

A) $6B
B) $106B
C) $1 trillion
D) $2.5 trillion

5. In the worked example, when does the $300 million deal pay off?

A) With better odds or a $5 billion drug
B) Always
C) Never, since royalties consume every dollar of profit on a licensed drug from China
D) At any peak sales

Module 6 — GLP-1 and the Obesity Revolution

The Largest Drug Story of the Decade

Recommended Reading / Reference

Reference: The SELECT, SURMOUNT, OASIS, ATTAIN, and TRIUMPH trial publications; Lilly's and Novo Nordisk's quarterly reports (2026); CMS on the Medicare GLP-1 Bridge (2026); Rodriguez and colleagues on discontinuation (*JAMA Network Open*, 2025)

6a. The Drugs

Drug	Company	Mechanism	Form	Weight loss in trials	2025 sales or status	US cash price (2026)
Ozempic and Wegovy (semaglutide)	Novo Nordisk	GLP-1 agonist	Weekly injection	About 15%	About $20.1B and $12.5B	Wegovy $249-329 a month; list price $675 from January 2027
Wegovy pill (oral semaglutide)	Novo Nordisk	GLP-1 agonist	Daily pill	13.6% at 64 weeks	About $500M in Q2 2026 (DKK 3.2B), its second quarter	$149-299 a month
Mounjaro and Zepbound (tirzepatide)	Eli Lilly	GLP-1 and GIP agonist	Weekly injection	About 21%	$23.0B and $13.5B	Cash prices cut in 2026; Medicare's bridge (6d)
Foundayo (orforglipron)	Eli Lilly	Small-molecule GLP-1 agonist	Daily pill	11-12% at 72 weeks	$98M in Q2 2026, its first quarter	$149-349 a month
Retatrutide	Eli Lilly	GLP-1, GIP, and glucagon agonist	Weekly injection	28.3% at 80 weeks (2026)	US filing planned for early 2027	—
CagriSema	Novo Nordisk	Amylin and GLP-1 agonists	Weekly injection	23.0%, against tirzepatide's 25.5% head to head	FDA decision due in the fourth quarter of 2026	—
MariTide	Amgen	GLP-1 agonist and GIP antagonist	Monthly injection	About 20% (Phase II)	Phase III	—
Metsera's drugs	Pfizer, which bought Metsera (Module 5)	GLP-1 agonist	Monthly injection	About 14% (Phase II)	Phase III	—
CSPC's monthly portfolio	AstraZeneca (2026 license: $1.2B upfront, $18.5B headline)	GLP-1 and GIP agonist	Monthly injection	Not yet tested in people	Entering Phase I	—
Generic semaglutide	Indian and other makers	GLP-1 agonist	Weekly injection	—	In India since the March 2026 patent expiry; approved in Canada and, since May 2026, in Brazil	A fraction of US prices

Company reports and trial publications; sales converted from Danish kroner where needed; company figures are claims.

6b. The Mechanism and the Trials

Glucagon-like peptide-1 (GLP-1) is a gut hormone that signals fullness, slows the emptying of the stomach, and prompts the release of insulin, and the drugs mimic it in longer-lasting forms. Developed for diabetes, with Ozempic approved in 2017, they produced weight loss in trials that no drug had come close to, and tirzepatide, which adds a second hormone called GIP, went further. In 2023 the SELECT trial showed a 20% reduction in heart attacks, strokes, and cardiovascular deaths among people with obesity, followed by evidence of benefit in kidney disease, sleep apnea, heart failure, and fatty liver disease, and early signs in addiction; a test in Alzheimer's failed (Module 12). Weight returns when the drugs stop, so treatment is indefinite. The side effects are mainly gastrointestinal, along with the loss of muscle and, rarely, pancreatitis. Outside trials, persistence is the weak point: in a 2025 study of 125,474 Americans, about half of those with diabetes and nearly two-thirds of those without it had stopped within a year.

6c. The Duopoly's End and the Pills

Novo and Lilly had the market to themselves, and a shortage, which the FDA declared over for tirzepatide in December 2024 and for semaglutide in February 2025, created a grey market of compounded copies. By 2026 the duopoly was a race that Lilly was winning. Tirzepatide's sales made it the world's best-selling medicine in 2025, ahead of Keytruda (Module 7), and Mounjaro alone sold $9.9 billion in the second quarter of 2026, up 91%. Novo's CagriSema fell short of tirzepatide head to head, its patents began to lapse abroad (table), and it cut jobs and guided to falling sales as its market value collapsed (Module 3). Pills then changed the market's shape. Novo's Wegovy pill leads in sales, while Lilly's Foundayo is a small molecule, cheaper to make in bulk than a peptide and free of the fasting rules that come with Novo's pill, and pills mean scale, price competition, and global reach. The next generation is in trials, led by Lilly's retatrutide and Novo's amycretin, which is in Phase III without pivotal results, along with monthly injections from Amgen, Pfizer, and AstraZeneca, while generics spread wherever patents have expired.

6d. Price, Coverage, and the World Beyond Medicine

Prices are falling fast. Cash prices fell through 2025 and 2026 (table), the companies' November 2025 most-favored-nation deals with the administration set a price of $245 a month for Medicare and Medicaid (Module 17), and Medicare's negotiated price for semaglutide follows (Module 17). Medicare cannot by law cover drugs for weight loss alone, so it opened the Medicare GLP-1 Bridge on July 1, 2026. Patients pay a $50 copay and Medicare pays the agreed price for Wegovy, Zepbound, and, by Lilly's account, Foundayo, for people with a body-mass index of 35 or more, or lower thresholds with conditions such as heart disease, prediabetes, or kidney disease. The bridge now runs through 2027, after CMS indefinitely delayed the Part D part of the BALANCE model that was to replace it; the Medicaid part began in May 2026. Most employers still restrict coverage. One in eight American adults had used one of the drugs by 2024, by a KFF poll, and the effects have reached beyond medicine: food companies cite lower sales of snacks and processed food, and the bariatric-surgery and sleep-apnea-device industries face a new competitor. Forecasters projected an obesity market of $100-150 billion a year by 2030, but with pills and generics its prices will fall as fast as its volume rises.

Module 6 Key Points

GLP-1 and the Obesity Revolution

• Tirzepatide sold $36.5 billion in 2025, overtaking Keytruda as the world's top-selling medicine; semaglutide's injections sold about $32.6 billion.

• The drugs mimic gut hormones; SELECT showed a 20% cut in major heart events in people with obesity.

• Weight returns when treatment stops, and about half of real-world users quit within a year.

• Pills arrived, priced from $149 a month, and retatrutide's 28% weight loss leads the next generation.

• Medicare's bridge program covers obesity drugs at a $50 copay from July 2026 through 2027.

Module 6 Quiz

Check Your Understanding

1. What did the SELECT trial show?

A) It showed the drugs cure diabetes.
B) It showed a 20% cut in major heart events in people with obesity.
C) It showed no effect on the heart.
D) It showed that the drugs cause weight gain in older people.

2. What share of real-world users stop GLP-1 drugs within a year?

A) Almost none of them stop within the first year.
B) About a fifth of them stop, mostly because of cost.
C) About half of them stop.
D) Nearly all of them stop within six months.

3. How much weight did retatrutide's top dose remove at 80 weeks?

A) It removed about 5%.
B) It removed about 50% of body weight in most patients.
C) It removed about 15%, the same as semaglutide.
D) It removed about 28%.

4. What does Medicare's GLP-1 bridge charge patients?

A) It charges $500.
B) It charges list price.
C) It charges a 20% coinsurance on the list price of about $1,000 a month, as in Part D.
D) It charges a $50 copay a month.

5. What did CagriSema's head-to-head trial against tirzepatide find?

A) It matched tirzepatide.
B) It fell short of tirzepatide's weight loss.
C) It beat tirzepatide by ten points of weight loss.
D) It was stopped early for safety problems in the liver.

Module 7 — Cancer

The Largest Therapeutic Area

Recommended Reading / Reference

Book: Siddhartha Mukherjee, *The Emperor of All Maladies*

Reference: IQVIA Institute, *Global Oncology Trends* (annual); ASCO and ESMO meeting reports (2025-26); the HARMONi trial publications (ivonescimab); 2026 reports from Merck, AstraZeneca, Johnson & Johnson, Novartis, and Summit Therapeutics

7a. The Approaches

Approach	Leading drugs (2025 sales)	Where it works best	2026 news
Chemotherapy, since the 1940s	Generics, the backbone of most regimens	Leukemias, lymphomas, and testicular cancer; combinations with newer drugs	Still most treatment worldwide
Targeted small molecules, since imatinib (2001)	Tagrisso ($7.3B), Kisqali ($4.8B), Ibrance, Verzenio, Calquence	Cancers driven by a known mutation, such as EGFR lung cancer	New pills against RAS, ROS1, and BCL-2 (7c)
Checkpoint inhibitors, since 2011	Keytruda (7b), Opdivo, Imfinzi ($6.1B), Tecentriq	Melanoma and lung, kidney, and bladder cancer; 20-40% of patients respond	Injections under the skin; the ivonescimab challenge (7b)
Other antibodies	Darzalex ($14.4B), Herceptin, Avastin	Myeloma, breast cancer, lymphoma	Biosimilars of the older ones
Antibody-drug conjugates	Enhertu ($2.8B to AstraZeneca, up 40%), Padcev, Trodelvy, Datroway	HER2 breast cancer, including the HER2-low type; bladder and lung cancer	Datroway's approval (7c)
Bispecific antibodies	Tecvayli ($670M), Talvey ($463M), Columvi, Epkinly	Myeloma and lymphoma; solid tumors emerging	Ivonescimab's FDA decision (7b)
CAR-T cell therapy	Carvykti ($1.9B), Yescarta, Breyanzi, Abecma	Relapsed blood cancers	Engineering inside the body; autoimmune disease (Module 9)
Radiopharmaceuticals	Pluvicto ($2.0B, up 43%), Lutathera ($816M)	Prostate and neuroendocrine tumors	Actinium-based successors; isotope supply
Hormonal therapy	Enzalutamide, abiraterone, tamoxifen	Breast and prostate cancer	Pills that destroy the estrogen receptor (7c)
Cancer vaccines	None approved; Moderna and Merck's intismeran in Phase III	Melanoma after surgery	Phase III met its main goal, by the makers' account (7c)

Company reports (2026); sales are company claims, and Enhertu's figure is AstraZeneca's booked share.

Cancer is the largest therapeutic area, worth about $250 billion in 2024 by IQVIA's count and about a third of the industry's pipeline. It is many diseases rather than one, its drugs command the highest prices, often $150,000-500,000 a year, and regulators accept more toxicity and faster paths for it, through accelerated approval above all (Module 2). The approaches have accumulated rather than replaced one another: most patients still receive chemotherapy, now combined with targeted, immune, or conjugate drugs chosen by the genetic profile of the tumor. Even so, cancer drugs have some of the lowest odds of success (Module 2), because tumors evolve around them and animal models predict human results poorly.

7b. Immunotherapy and the Challenge From China

Checkpoint inhibitors are antibodies that release brakes on the immune system, the PD-1 and CTLA-4 proteins that tumors exploit to switch off the T-cells that would attack them, and the discoveries behind them won James Allison and Tasuku Honjo the 2018 Nobel Prize. They turned metastatic melanoma from a death sentence into a disease that some patients survive for a decade, and they changed the treatment of lung, kidney, and bladder cancer. Merck's Keytruda sold $31.6 billion in 2025, second only to tirzepatide (Module 6). With Keytruda Qlex, its injection under the skin, it sold $8.4 billion in the second quarter of 2026, of which Qlex was $463 million. New combinations approved in 2026, with Padcev in bladder cancer, Welireg in kidney cancer, and Trodelvy in triple-negative breast cancer, extend its reach as its patent cliff approaches (Module 5).

The most serious challenge to Keytruda came from China. Akeso's ivonescimab is a bispecific antibody that blocks both PD-1 and VEGF, a signal that tumors use to grow blood vessels, and it was licensed outside China to Summit Therapeutics (Module 14). In 2024 it became the first drug to beat Keytruda head to head in a Phase III trial, HARMONi-2 in China, where it nearly doubled the time before PD-L1-positive lung cancer progressed, and Pfizer, Bristol Myers Squibb, and Merck have since licensed Chinese rivals of the same design. Its supporters point to the size of that result, a hazard ratio of 0.51 against the world's best-selling cancer drug, and to a mechanism that hits two pathways at once. Its skeptics answer that progression-free survival is a surrogate, that Chinese trials differ from Western practice, and that the drug has yet to show that Western patients live longer. The evidence is now split. Akeso's HARMONi-6 trial in China reported in May 2026 that ivonescimab cut the risk of death in squamous lung cancer by 34% against another PD-1 antibody, tislelizumab, when each was given with chemotherapy, a statistically significant result. In Summit's global HARMONi trial, in lung cancer that had resisted EGFR inhibitors, the survival hazard ratio for Western patients was 0.76 at the June 2026 cutoff, a 24% lower risk of death that Summit did not report as statistically significant. The FDA accepted Summit's application based on that trial in January 2026 and is due to decide by November 14, 2026. HARMONi-3, which tests the drug against Keytruda with chemotherapy as a first treatment, reports progression-free survival for squamous lung cancer in the second half of 2026 and for the non-squamous type in the first half of 2027. This course's reading is that ivonescimab has shown in Chinese patients that it can slow lung cancer better than Keytruda and extend survival against a rival PD-1 drug, but not yet that it helps Western patients live longer, so the challenge is real but unproven until HARMONi-3 reports.

7c. Conjugates, New Pills, Cell Therapy, and Vaccines

Antibody-drug conjugates are the fastest-growing class. Enhertu's expansion into HER2-low breast cancer, a type once thought to lack the target, multiplied its market, Datroway won approval in 2026 as a first treatment for triple-negative breast cancer, and AbbVie's Decnupaz was approved for a rare blood cancer in May 2026. Many of the conjugates now in development were licensed from Chinese companies (Module 14). Small molecules have also had a strong year. Pfizer and Arvinas's Veppanu (State of the Art) and AstraZeneca's Etcamah, approved in September 2026, are pills that destroy the estrogen receptor in breast cancers that have mutated to escape hormone therapy. Rasonque, Revolution Medicines' inhibitor of the RAS proteins that drive most pancreatic cancers and were long called undruggable, was approved for metastatic pancreatic cancer (State of the Art). The year also brought pills for ROS1-driven lung cancer (Nuvalent's Jideytro, July), mantle cell lymphoma (BeOne's Beqalzi, May), and myeloma (Bristol Myers Squibb's Zenbexus, August).

CAR-T cell therapy, a patient's own T-cells engineered to attack a tumor, produces lasting remissions in 40-60% of relapsed blood cancers, but it costs $400,000-500,000, takes weeks to make, and can trigger dangerous immune reactions that need a hospital. It has not yet worked in solid tumors, where two other T-cell therapies were approved in 2024, Amtagvi for melanoma and Tecelra for a rare sarcoma. Its next forms are made from donor cells or engineered inside the body, an approach that AbbVie, AstraZeneca, and Gilead each bought into in 2025, and its surprise has come in autoimmune disease (Module 9).
Personalized cancer vaccines, mRNA that encodes the mutations of a patient's own tumor, are the other frontier. Moderna and Merck's intismeran, given with Keytruda after surgery for melanoma, cut the risk of recurrence or death by about half in a Phase II trial, with five-year data presented in 2026. In August 2026 the two companies announced that its Phase III trial, of 1,137 patients, had met its main goal of reducing recurrence or death, though they had not released the figures. Its full Phase III results, and BioNTech's, will decide whether oncology becomes mRNA's second act (Module 11).

Module 7 Key Points

Cancer

• Cancer is many diseases and the largest therapeutic area, about $250 billion a year, where new approaches add to chemotherapy rather than replace it.

• Keytruda sold $31.6 billion in 2025, second to tirzepatide, and is extending its reach with new combinations as its cliff nears.

• Ivonescimab beat Keytruda on progression-free survival in China in 2024 and extended survival against a rival there in 2026, not yet in Western patients.

• New 2026 pills destroy the estrogen receptor in resistant breast cancer and block RAS, the pancreatic cancer driver long called undruggable.

• CAR-T gives lasting remissions in 40-60% of relapsed blood cancers but costs $400,000-500,000 and has not yet worked in solid tumors.

• A personalized mRNA vaccine halved melanoma recurrence in Phase II, and its makers say it met its Phase III goal in August 2026.

Module 7 Quiz

Check Your Understanding

1. Why is cancer the industry's largest therapeutic area?

A) It is many diseases, its drugs command the highest prices, and regulators allow faster paths.
B) It is a single disease with one target.
C) Its drugs are the cheapest to develop, so companies can run more trials than elsewhere.
D) Its patents last longer.

2. What has ivonescimab not yet shown in Western patients?

A) Faster tumor shrinkage
B) Activity in lung cancer
C) Longer survival
D) A licensing deal outside China

3. What do Veppanu and Etcamah do?

A) Block RAS
B) Train the immune system against a tumor
C) Carry a toxic payload to HER2
D) Destroy the estrogen receptor in breast cancers that resist hormone therapy

4. Where does CAR-T produce lasting remissions in 40-60% of patients?

A) Solid tumors
B) Melanoma
C) Relapsed blood cancers
D) Early-stage lung cancer

5. What will decide whether oncology becomes mRNA's second act?

A) Their price, since personalized vaccines must be made for each patient at a cost of millions
B) Phase III results
C) COVID vaccine sales
D) Moderna's share price

Module 8 — Heart, Metabolic, and Kidney Disease

The Diseases That Kill the Most People

Recommended Reading / Reference

Reference: The FOURIER, CORALreef, Lp(a)HORIZON, EMPA-REG OUTCOME, DAPA-HF, and FLOW trial publications; the Cholesterol Treatment Trialists' meta-analyses; Burgess and colleagues on Lp(a) genetics (*JAMA Cardiology*, 2018); 2026 reports from Merck, Novartis, Amgen, and AstraZeneca

8a. Cholesterol: From Statins to Pills

Class	How it works	Example	LDL reduction	Status in 2026
Statins	Block the liver enzyme that makes cholesterol	Atorvastatin (generic)	30-50%	The foundation, at about $50 a year
Ezetimibe	Blocks absorption from the gut	Generic	15-20%	An add-on
PCSK9 antibodies	Block the protein that destroys the liver's LDL receptors	Repatha (Amgen), Praluent (Regeneron)	50-60%	Outcomes proven (FOURIER)
PCSK9 silencing	Silences the PCSK9 gene with two injections a year	Leqvio (Novartis)	About 50%	The first RNA drug for a mass disease
Oral PCSK9	A pill that blocks PCSK9	Lipfendra (Merck)	56-59% more than placebo	Approved (State of the Art); outcomes trial under way
Bempedoic acid	Acts upstream of statins in the same pathway	Nexletol (Esperion)	About 20%	For people who cannot take statins
Lp(a) lowering	Silences lipoprotein(a), a genetic risk factor that statins do not touch	Pelacarsen (Novartis), olpasiran (Amgen), lepodisiran (Lilly)	80-95% of Lp(a)	The first outcomes trial failed (8b)

Trial publications and company reports; reductions are typical, and Lipfendra's are company claims.

Cardiovascular disease kills more people than anything else, about 18-20 million a year, and its drugs are the industry's oldest mass market and its most generic. Statins, taken by about 200 million people, set the baseline (table), and each fall of 1 mmol/L in LDL cholesterol cuts major heart events by about a fifth, so every later advance has had to justify its price against a generic. The PCSK9 antibodies (2015) sold poorly at $14,000 a year until their prices fell by more than half, and Novartis's Leqvio silences the same gene. Merck's Lipfendra, a pill that does what the antibodies do, could become the first new mass-market cholesterol drug since the statins.

8b. Lipoprotein(a): The First Test Fails

Lipoprotein(a), or Lp(a), is a cholesterol-carrying particle whose level is set almost entirely by genes. About a fifth of people have enough of it to raise their risk of heart attack and stroke, and no statin, diet, or exercise lowers it. Drugs that silence its gene cut it deeply (table), and their outcomes trials were the largest untested hypothesis in cardiology. On September 4, 2026, Novartis announced that the first had failed: in Lp(a)HORIZON, 8,323 patients with heart disease and high Lp(a) took pelacarsen, an antisense drug, or a placebo, and although the drug lowered Lp(a) it did not significantly reduce heart attacks, strokes, deaths, or urgent procedures.

Optimists say the genetics are unambiguous and that pelacarsen's cut of about 80% may have been too small, since a 2018 genetic analysis estimated that Lp(a) must fall by about 100 mg/dL to match the benefit of lowering LDL by 1 mmol/L. They add that patients already taking GLP-1, SGLT2, and PCSK9 drugs leave less risk to remove. Pessimists say that a large, well-run trial in the patients most likely to benefit found nothing, and that the newer drugs share the hypothesis even if they lower Lp(a) further. The evidence is incomplete: Novartis has not released the full data, and Amgen's olpasiran, a small interfering RNA (siRNA) drug that cuts Lp(a) by about 95%, completes its outcomes trial of 7,297 patients around March 2028, with Lilly's once-a-year lepodisiran behind it. This course's reading is that the failure weakens the hypothesis without killing it, and that the siRNA trials, not pelacarsen's, will decide whether Lp(a) becomes a mass market.

8c. Heart Failure, Blood Pressure, and the SGLT2 Accident

The decade's most consequential cardiovascular discovery was an accident. SGLT2 inhibitors, Boehringer and Lilly's Jardiance and AstraZeneca's Farxiga, were developed as diabetes drugs that make the kidneys excrete glucose. Regulators required trials to show that they were safe for the heart, and the trials found instead that they cut hospitalization for heart failure by about a third and slowed kidney disease, in people with and without diabetes. They are now standard treatment for heart failure and chronic kidney disease, both are among Medicare's first negotiated drugs (Module 17), and Farxiga's first US generics were approved in April 2026. Heart failure's other modern drugs, Novartis's Entresto, now generic (Module 5), Bristol Myers Squibb's Camzyos for an inherited thickening of the heart muscle, and the GLP-1s, which helped the form of heart failure in which the heart stiffens, have made a disease that killed half its patients within five years a managed condition for many. Blood pressure, the largest risk factor of all, gained a new class of drug in May 2026, when the FDA approved AstraZeneca's Baxfendy (baxdrostat), which blocks the making of the hormone aldosterone, for patients whose pressure stays high on other drugs. Diabetes gained weekly basal insulins, Novo's Awiqli and Lilly's Onswik (State of the Art), in place of daily injections.

8d. Kidney Disease and the Convergence

Kidney disease affects about 850 million people worldwide, most of them undiagnosed, and its end stage, dialysis, costs about $90,000 per patient a year and Medicare about $50 billion in all. The SGLT2 drugs, Bayer's Kerendia, and the GLP-1s, whose FLOW trial showed semaglutide cut the progression of kidney disease by 24%, are the first drugs in decades to slow it, which is why the dialysis companies DaVita and Fresenius are among the businesses that the obesity drugs threaten. A rarer kidney disease, IgA nephropathy, has drawn a cluster of new drugs, including Vera Therapeutics' Trutakna (atacicept), approved in July 2026 to reduce protein in the urine. The convergence is the point. Obesity, diabetes, heart failure, kidney disease, fatty liver disease, and sleep apnea are increasingly treated as one metabolic syndrome with one set of drugs, the GLP-1 and SGLT2 classes. Fatty liver disease shows how fast the overlap moves: Madrigal's Rezdiffra was the first approved drug for its serious form in 2024, Wegovy followed in August 2025, and Novo's pill awaits an FDA decision in early 2027. The companies that own these classes, Lilly, Novo, AstraZeneca, and Boehringer, own one of the largest markets in medicine.

Module 8 Key Points

Heart, Metabolic, and Kidney Disease

• Statins cut LDL by 30-50% for about $50 a year, so every newer cholesterol drug, including Merck's new PCSK9 pill, must justify its price.

• The first Lp(a) outcomes trial, of Novartis's pelacarsen, failed in September 2026; Amgen's and Lilly's stronger siRNAs are now the test.

• SGLT2 inhibitors, built for diabetes, were found in safety trials to cut heart-failure hospitalization by about a third and slow kidney disease.

• Semaglutide cut kidney-disease progression by 24% in FLOW, threatening a dialysis business that costs Medicare about $50 billion a year.

• Obesity, diabetes, heart, kidney, and liver disease increasingly share one set of drugs, the GLP-1 and SGLT2 classes.

Module 8 Quiz

Check Your Understanding

1. Why must every new cholesterol drug justify itself against statins?

A) Statins are generic and cut LDL by 30-50%.
B) Statins must be injected by a nurse each week.
C) Statins are rarely prescribed.
D) Statins work only in people who already have heart disease.

2. What did the Lp(a)HORIZON trial of pelacarsen find in September 2026?

A) It cut heart attacks by half.
B) It failed to lower Lp(a).
C) It was stopped early because the drug harmed the livers of many patients
D) It lowered Lp(a) but did not significantly reduce heart attacks, strokes, or deaths.

3. Where were the SGLT2 inhibitors' heart benefits found?

A) In mice
B) In safety trials
C) In trials for gout
D) In trials designed for heart failure

4. Which company's siRNA completes its Lp(a) outcomes trial around March 2028?

A) Novartis
B) Pfizer, after buying the rights to the drug from a Chinese biotech in 2025
C) Amgen
D) Novo Nordisk

5. Why do the GLP-1 drugs threaten the dialysis industry?

A) Semaglutide slowed kidney disease by 24% in the FLOW trial.
B) They cause the kidneys to fail sooner in diabetics.
C) They replace dialysis machines.
D) They cost more than dialysis, so insurers have stopped paying for both treatments.

Module 9 — Immunology and Inflammation

The Franchise Business

Recommended Reading / Reference

Reference: 2025 annual and 2026 quarterly reports from AbbVie, Sanofi, Johnson & Johnson, and Lilly; the American College of Rheumatology and American Academy of Dermatology guidelines; Müller and colleagues on CAR-T in autoimmune disease (*New England Journal of Medicine*, 2024)

9a. The Diseases and the Drugs

Disease	US patients	Drug classes	Leading drugs (2025 sales)	Note
Rheumatoid arthritis	1.5M	TNF, IL-6, JAK	Humira, Enbrel, Rinvoq, Actemra	The first biologic market
Psoriasis and psoriatic arthritis	8M	IL-17, IL-23, TNF; oral TYK2, PDE4, and IL-23	Skyrizi ($17.6B), Tremfya ($5.2B), Cosentyx, Taltz, Sotyktu, Icotyde	The most competitive
Crohn's disease and ulcerative colitis	3M	TNF, IL-23, integrin, JAK, S1P	Skyrizi, Stelara ($6.1B, falling to biosimilars), Entyvio, Rinvoq	TL1A next (9c)
Atopic dermatitis (eczema)	30M, 7M of them moderate to severe	IL-4/13, IL-13, JAK, OX40	Dupixent (€15.7B, about $17.7B), Rinvoq, Adbry, Ebglyss	Dupixent's franchise
Asthma and COPD	25M and 15M	IL-5, IL-4/13, TSLP	Dupixent, Nucala, Tezspire, Fasenra	COPD the newest frontier
Lupus	300K	B-cell, interferon	Benlysta, Saphnelo; CAR-T in trials	The hardest (9c)
Multiple sclerosis	1M	B-cell depletion, S1P	Ocrevus, Kesimpta	BTK inhibitors stumbled (9c)
Alopecia, vitiligo, hidradenitis, and rarer diseases	Millions	JAK, IL-17, IL-4/13	Olumiant, Litfulo, Opzelura, Cosentyx	New 2026 drugs (9c)
All immune-mediated disease	About 50M		About $120B a year worldwide	—

Company reports (2026; sales are company claims, and the dollar figure for Dupixent is converted from euros); patient counts are approximate.

Immune-mediated diseases, in which the body attacks its own tissues, form one of the industry's largest markets (table) and the one where biologics first proved their worth. Humira and the other TNF blockers turned rheumatoid arthritis from a crippling disease into a managed one in the 2000s, and each later class has been more targeted. The same immune pathways drive many of these diseases, so a drug approved for one expands, indication by indication, into a franchise: Dupixent went from eczema to asthma to COPD, and Skyrizi from psoriasis to Crohn's disease and colitis. A company that owns a pathway owns a decade.

9b. Humira's Succession and the Classes

Humira, AbbVie's TNF blocker, was the world's best-selling drug for a decade, peaking at about $21 billion in 2022, and its patent thicket held off US biosimilars for years (Module 5). AbbVie's succession is the industry's case study. It developed Skyrizi, an IL-23 antibody, and Rinvoq, an oral JAK inhibitor for arthritis, eczema, and colitis, launched them years before the cliff, priced them above Humira, and moved patients

across. In 2025 the two sold $25.9 billion between them, Rinvoq $8.3 billion of it, more than Humira at its peak, while Humira's own sales fell as biosimilars arrived (Module 4). Sanofi and Regeneron's Dupixent, up 25% in 2025, is the other giant, essentially tied with Skyrizi as the top immunology drug.

The classes are named for the signal they block. IL-23 blockers (Skyrizi, Tremfya, and Stelara, which also blocks IL-12) treat psoriasis and bowel disease, and IL-17 blockers (Cosentyx, Taltz, Bimzelx) treat psoriasis and spondylitis. IL-4 and IL-13 blockers (Dupixent, Ebglyss) treat the allergic diseases, and the JAK inhibitors (Rinvoq, Xeljanz, Olumiant) are pills that have carried an FDA warning on heart, cancer, and clotting risks since a 2021 safety trial. Pills are spreading. Otezla (2014) was an early oral option for psoriasis, Sotyktu (2022) became the first TYK2 inhibitor, and Johnson & Johnson's Icotyde, developed with Protagonist, is the first pill aimed at the IL-23 pathway (State of the Art).

9c. The Next Wave and the Setbacks

TL1A, a signal that drives inflammation and scarring in the gut, drew immunology's largest bets: Merck's purchase of Prometheus (Module 5), Roche's $7.1 billion purchase of Telavant in 2023, and a Sanofi and Teva antibody, duvakitug, that began four Phase III trials in Crohn's disease and colitis in early 2026. If the trials succeed, TL1A will add a new mechanism for bowel disease. CAR-T's results in lupus, where patients given a single infusion have stayed in remission without drugs, would be the first cure-like result in autoimmunity if they hold in larger trials. The year's approvals widened the field, mostly to rarer diseases: brepocitinib (Lisraya) for dermatomyositis in August 2026, veligrotug (Lumvoa) for thyroid eye disease in June, and difamilast (Adquey), a cream for milder eczema, in February.

Multiple sclerosis supplied the setback. The BTK inhibitors, meant to slow the disability that accumulates in its progressive forms, stumbled when the FDA rejected Sanofi's tolebrutinib in December 2025 and a second Phase III trial missed its goal, and Sanofi wrote down €1.7 billion. Immunology's economics are the mirror of oncology's: chronic diseases treated for decades in millions of patients at $50,000-90,000 a year, with the biosimilar cliff reaching each class in turn (Module 5).

Module 9 Key Points

Immunology and Inflammation

• Immune-mediated diseases form a market of about $120 billion a year, where one pathway's drug expands disease by disease into a franchise.

• AbbVie replaced Humira with Skyrizi and Rinvoq, which sold $25.9 billion together in 2025, more than Humira at its peak.

• Dupixent sold about $17.7 billion in 2025, essentially tied with Skyrizi as the top immunology drug.

• Pills are spreading: Icotyde is the first oral drug aimed at IL-23, while JAK pills carry an FDA safety warning.

• TL1A is the next bowel-disease bet; the BTK inhibitors stumbled in multiple sclerosis after an FDA rejection in December 2025.

Module 9 Quiz

Check Your Understanding

1. Why do immunology drugs become franchises?

A) They are cheap to make
B) They are taken once in a lifetime, so each patient is treated only one time
C) Their patents last longer than other drugs' patents do
D) The same pathways drive many diseases

2. How did AbbVie survive Humira's cliff?

A) By winning a court ruling that extended Humira's patents to 2030
B) With successor drugs
C) By cutting Humira's price below the biosimilars' prices
D) By selling Humira to a generic maker

3. What did the FDA do with Sanofi's tolebrutinib in December 2025?

A) Approved it
B) Approved it for all forms of multiple sclerosis after a priority review lasting six months
C) Rejected it for a progressive form of MS
D) Delayed it

4. What did Skyrizi and Rinvoq sell together in 2025?

A) $25.9 billion, more than Humira at its peak
B) $4.5 billion
C) About $10 billion
D) $60 billion, AbbVie's total

5. Which drug is the first pill aimed at the IL-23 pathway?

A) Icotyde
B) Sotyktu, a TYK2 drug
C) Rinvoq, a JAK pill
D) Otezla, from 2014

Module 10 — Genetic Medicine

The Therapies That Edit, Replace, or Silence Genes

Recommended Reading / Reference

Book: Walter Isaacson, *The Code Breaker*

Reference: The 2025 *New England Journal of Medicine* report of the first personalized base edit and the Children's Hospital of Philadelphia's one-year update (2026); the HAELO trial results (Intellia, 2026); the FDA's Elevidys safety communications (2025); Vertex's and Alnylam's 2026 reports; ICER's gene-therapy reviews

10a. Gene Editing

CRISPR is a bacterial defense system that Jennifer Doudna and Emmanuelle Charpentier turned in 2012 into a tool for cutting DNA at a chosen sequence, work that won them the 2020 Nobel Prize, and it became a medicine with Vertex and CRISPR Therapeutics' Casgevy (State of the Art). A patient's stem cells are removed, edited to switch on fetal hemoglobin, and returned after chemotherapy clears the bone marrow, and the treatment has ended the crises of sickle-cell disease, or the transfusions of beta-thalassemia, in more than nine in ten patients treated. It costs $2.2 million in the United States and requires weeks in a hospital, and it sold $76 million in the second quarter of 2026, about 35 treatments at the US price.

The field's founding scandal came first. In November 2018 the Chinese scientist He Jiankui announced the birth of twin girls whose embryos he had edited in secret to disable CCR5, a gene that HIV uses to enter cells, although the edits were imperfect and the girls had no medical need. A third edited child followed. Scientists worldwide condemned him, a Chinese court jailed him for three years in 2019, and China made such editing a crime in 2020, while the WHO set up a registry and leading scientists called for a global moratorium on heritable editing. No further edited babies have been reported, and the case drew the line that the field still polices: editing a patient's own cells, as Casgevy does, is medicine, while editing an embryo changes every descendant and remains off limits.

The newest work edits genes inside the body. In 2025 doctors at the Children's Hospital of Philadelphia treated an infant, KJ Muldoon, who had a fatal inherited liver disorder, with a base editor designed and made for him alone, given in three infusions from February to April and published in May. A year later he was walking, talking, and tolerating more protein, though the hospital says the treatment is not a cure. The FDA responded with a 'plausible mechanism' pathway in November 2025 and, in February 2026, a framework under which every version of one editor counts as a single drug, so that success in as few as 5-10 patients could support approval of the platform. Intellia's lonvo-z, a single injection for hereditary angioedema, gave the first Phase III results for any in-body editor in April 2026: by Intellia's account, attacks fell 87% against placebo, and 62% of treated patients were free of attacks without other preventive drugs (State of the Art). The same company's amyloidosis editor, nex-z, shows the risk. A patient in his 80s died of liver injury in late 2025, the FDA halted both of its Phase III trials, and Intellia said in August 2026 that enrollment had resumed. Lilly bought Verve, which edits a cholesterol gene, for up to about $1.3 billion in 2025, and base and prime editing, which change single letters of DNA without cutting both strands, are the next generation.

10b. Gene Therapy

Therapy	Company	Disease	Approved	Price	Status
Luxturna	Spark (Roche)	Inherited retinal blindness	2017	$850,000	The first US in-body gene therapy for an inherited disease; modest sales
Zolgensma	Novartis	Spinal muscular atrophy	State of the Art	About $2.1M	The commercial success, about $1.2B a year; a spinal-injection form, Itvisma, approved in 2025
Zynteglo, Skysona, Lyfgenia	bluebird bio	Thalassemia, a brain disease (CALD), sickle cell	2022-23	$2.8-3.1M	The pioneer, sold to private equity in 2025 for about $30M upfront
Hemgenix; Roctavian	CSL; BioMarin	Hemophilia B; hemophilia A	2022-23	$3.5M; $2.9M	Little uptake; Pfizer abandoned its rival, Beqvez, in 2025
Elevidys	Sarepta (Roche outside the US)	Duchenne muscular dystrophy	Accelerated (10c)	$3.2M	Restricted after deaths (10c)
Kebilidi; Lenmeldy	PTC; Orchard (Kyowa Kirin)	AADC deficiency; metachromatic leukodystrophy	2024	About $4M each	Ultra-rare diseases, orphan economics
Kresladi	Rocket Pharmaceuticals	Leukocyte adhesion deficiency	March 2026, accelerated	Not disclosed	The first gene therapy for the disease
Fayuvi	Ultragenyx	Sanfilippo syndrome type A	State of the Art	Not disclosed	The first drug of any kind for the disease

FDA records and company statements; prices are US list prices.

Gene therapy delivers a working gene, usually inside a harmless virus, to cells that lack it. Its record is a paradox: it has halted spinal muscular atrophy, restored sight, and stopped bleeding in hemophilia, yet it has failed commercially for almost everyone but Zolgensma. Prices of $2-4 million for a single treatment, tiny patient populations, insurers' reluctance, difficult manufacturing, and the fact that a cure sells only once have produced the wreckage in the table. Optimists say the business can be rebuilt: an in-body editor is a drug made in a factory rather than a procedure in a transplant center, platform approvals let one product serve many mutations, and outcomes-based contracts let payers spread a multimillion-dollar price over the years in which the cure keeps working. Pessimists say each of those fixes is still a promise, that large companies such as Pfizer have left, and that investors have retreated after bluebird's sale for a fraction of the money it raised. The evidence is mixed: Casgevy's sales rose 151% in a year but remain small, while Lilly and AbbVie paid billions for in-body editing and cell engineering (10a and Module 7). This course's reading is that the science has outrun the business, and that the business will be rebuilt around in-body editing and platform approvals rather than rescued for the viral gene therapies of the 2010s.

10c. Elevidys and the Limits of a Surrogate

Sarepta's Elevidys, for Duchenne muscular dystrophy, a fatal muscle-wasting disease of boys, is the case that defines the modality's risks. The FDA granted it accelerated approval in 2023 for four- and five-year-olds over the objections of its own reviewers, on a surrogate: the production of a shortened form of the missing protein, dystrophin. In 2024 it widened the label to older boys, including those who could no longer walk, although the confirmatory trial had missed its primary goal. In 2025 two teenagers who could no longer walk died of acute liver failure, and a third patient died in a trial of a related Sarepta therapy for another muscle disease. Shipments were halted, restricted, and resumed, and in November 2025 the FDA

added a boxed warning, limited the therapy to patients aged four and older who can walk, and required a study of about 200 patients with a year of liver monitoring. More than 760 patients who could walk had been treated without a death by September 2025, by Sarepta's count, and sales fell 65% in a year, to $98 million in the second quarter of 2026. The lesson is that accelerated approval in gene therapy carries risks that a surrogate cannot measure, and that a handful of deaths can change a modality's future; the wider debate over the pathway is in Module 16.

10d. RNA Drugs

RNA medicines, antisense strands and small interfering RNA (siRNA) that silence a gene's message rather than edit the gene, are the genetic modality that has worked commercially. Alnylam's Amvuttra, for transthyretin amyloidosis, sold $2.3 billion in 2025 after its heart-disease approval (State of the Art), and Alnylam guides its amyloidosis drugs to $4.4-4.7 billion in 2026 (company guidance). Novartis's Leqvio (Module 8) and Biogen and Ionis's Spinraza are the other leaders, and 2025 brought approvals for hemophilia (Sanofi's Qfitlia), hereditary angioedema (Ionis's Dawnzera), and a rare disorder of blood fats (Arrowhead's Redemplo). GSK's bepirovirsen, from Ionis, functionally cured about a fifth of patients with chronic hepatitis B in two Phase III trials, against none on placebo, by GSK's account, won its first approval in Japan in August 2026, and awaits an FDA decision. The advantages of these drugs are reversibility, doses every three to six months, and manufacture as chemicals rather than in living cells; their limit is delivery, since most reach the liver easily and other organs with difficulty. mRNA, which instructs cells to make a protein, is covered as vaccines in Module 11 and as cancer therapy in Module 7.

10e. The Access Problem

Genetic medicine's defining tension is that its cures exist and most of its patients cannot reach them. About 7.7 million people worldwide have sickle-cell disease, most of them in Africa, where the transplant centers that Casgevy requires are rare, and Medicaid covers about half of the roughly 100,000 American patients. The CMS Cell and Gene Therapy Access Model, launched in 2025, lets state Medicaid programs pay for sickle-cell gene therapies under outcomes-based contracts, and the FDA's framework for bespoke editors (10a) is the first regulatory answer to the thousands of ultra-rare mutations that no company will develop a drug for. The industry's bet is that in-body editing and manufacturing at scale will cut costs by an order of magnitude in the 2030s; until then, genetic medicine is a proof of concept with a price tag.

Module 10 Key Points

Genetic Medicine

• Casgevy, the first CRISPR medicine, ends sickle-cell crises in nine in ten patients but costs $2.2 million and reaches few.

• He Jiankui's edited babies of 2018 drew the field's hardest line: edit a patient's own cells, never an embryo.

• In-body editing arrived: a bespoke editor treated an infant in 2025, and lonvo-z cut angioedema attacks 87% in Phase III, by Intellia's account.

• Gene therapy works scientifically but has failed commercially for nearly all but Zolgensma, at $2-4 million a treatment.

• Elevidys won accelerated approval on a surrogate; two deaths in 2025 brought a boxed warning and a narrower label.

• RNA-silencing drugs are the genetic modality that sells: Amvuttra made $2.3 billion in 2025.

Module 10 Quiz

Check Your Understanding

1. How does Casgevy treat sickle-cell disease?

A) A daily pill
B) A blood transfusion
C) A viral gene injection
D) Edited stem cells, returned to the patient

2. What did He Jiankui do in 2018?

A) He won the Nobel Prize for inventing CRISPR, together with two American colleagues
B) He edited human embryos
C) He cured sickle cell
D) He led the first approved CRISPR trial of an in-body editor

3. What did lonvo-z achieve in its 2026 Phase III trial?

A) No benefit
B) A cure for sickle cell
C) An 87% cut in angioedema attacks
D) Approval in every major market within a month of the results, a first for gene editing

4. What did the FDA add to Elevidys's label in November 2025?

A) A price cap set by Medicare at $1 million per patient for all ages
B) Approval for all ages, including boys who cannot walk
C) A full withdrawal of the therapy
D) A boxed warning

5. Why have RNA-silencing drugs succeeded where gene therapy has struggled?

A) They cure the disease permanently with a single dose for life
B) They are free
C) They are reversible and dosed every few months
D) They work equally well in every organ of the body, not only the liver, and need no injections

Module 11 — Vaccines and mRNA

The Technology That Ended a Pandemic, and the Policy Turn Against It

Recommended Reading / Reference

Book: Gregory Zuckerman, *A Shot to Save the World*

Reference: The 2023 Nobel Prize citation (Karikó and Weissman); Watson and colleagues on deaths averted (*Lancet Infectious Diseases*, 2022); CDC and ACIP records (2025-26); the March 2026 order in *American Academy of Pediatrics v. Kennedy*; 2025 reports from Merck, Pfizer, GSK, and Moderna

11a. The Race

The COVID-19 vaccines were the fastest ever made. Chinese scientists published the virus's genetic sequence in January 2020, Moderna had designed its vaccine within days, and by December 2020 regulators had authorized Pfizer and BioNTech's vaccine and then Moderna's, eleven months from sequence to shot, with adenovirus vaccines from AstraZeneca and Oxford and from Johnson & Johnson close behind. Three things made the speed possible: decades of earlier research on mRNA and on coronaviruses, Operation Warp Speed's roughly $18 billion of US funding and guaranteed purchases, and manufacturing at risk, in parallel with trials rather than after them. The mRNA platform rested on the work of Katalin Karikó and Drew Weissman, who found how to keep synthetic mRNA from triggering the immune system and won the 2023 Nobel Prize for it.

The results were historic. The vaccines averted an estimated 14-20 million deaths in their first year, by a 2022 study in *The Lancet Infectious Diseases*, and Pfizer, BioNTech, and Moderna sold more than $100 billion of them in 2021-22. The failure was distribution: by the end of 2021 most people in rich countries had been fully vaccinated, while fewer than one in ten people in low-income countries had received a single dose. The lesson is what a year can do when every incentive points the same way, and how quickly a triumph can be undone politically (11c).

11b. The Collapse and the Second Acts

The commercial collapse followed the pandemic's end. COVID vaccine sales fell by about 90% from their peak, to $4.4 billion for Pfizer's Comirnaty in 2025, and Moderna's total revenue fell 40% that year, to $1.9 billion, most of it still from COVID. Uptake of updated shots fell to about a fifth of American adults, Moderna's market value fell from nearly $200 billion in 2021 to under $15 billion in 2025, and its RSV vaccine sold little. The platform's second acts have been slower than the boom had priced, but one has now arrived: Moderna's mFLUSIVA, the first mRNA flu vaccine, for adults aged 50 and older (State of the Art). The FDA had refused to review the application in February 2026, objecting to the comparison vaccine used in older patients, reversed itself about a week later, and approved it after its advisers voted unanimously in favor in June. Cancer vaccines are the other test (Module 7).

11c. The US Policy Upheaval

Date	Action
February 2025	Robert F. Kennedy Jr., a longtime vaccine critic, confirmed as Secretary of Health and Human Services
May 2025	Kennedy removes COVID vaccines from CDC recommendations for healthy children and pregnant women without a review by the CDC's advisers; HHS cancels Moderna's award of about $766M for an H5N1 bird-flu vaccine
June 2025	All 17 members of the CDC's vaccine advisory committee (ACIP) dismissed and replaced with the secretary's appointees, several of them vaccine critics
August 2025	The federal research agency BARDA winds down 22 mRNA projects worth about $500M and funds no new ones; the FDA limits COVID vaccines to people 65 and older and those at high risk; the CDC director, Susan Monarez, is fired
September 2025	West Coast and Northeast states form alliances to issue their own recommendations; medical societies publish their own schedules
December 2025	The new ACIP votes 8-3 to end the universal hepatitis B dose at birth for infants of mothers who test negative
January 2026	The acting CDC director's memo, issued without ACIP, moves vaccines including COVID, flu, hepatitis B, and rotavirus to shared decision-making, rolling back nearly half of childhood recommendations
March 2026	A federal court stays the January memo, 13 ACIP appointments, and all of the new committee's votes, finding it likely not 'fairly balanced' under federal law; the earlier schedule returns; the government appeals
2025-26	Measles: 2,289 US cases and 3 deaths in 2025, then 4,080 cases by October 8, 2026, a 35-year high; the Pan American Health Organization reviews US elimination status in November 2026

Federal records, court filings, CDC data, and press reports.

The United States, which funded and built the pandemic's vaccines, turned against them in policy within five years. Kennedy and his appointees argue that the old advisory committee was too close to manufacturers, that some recommendations, such as a hepatitis B shot for every newborn, went beyond the evidence for low-risk infants, and that parents should decide more for themselves. Medical societies, most former officials, and the court answer that the schedule rests on decades of safety data, that the changes bypassed the reviews on which the system depends, and that a committee with little vaccine expertise was not lawfully constituted. The evidence on outcomes favors the changes' critics so far: measles cases have surged (table), and the share of kindergartners exempted from vaccines reached a record 4.2% in the 2025-26 school year, up from 3.6% the year before. This course's reading is that the changes were made around the evidence-review system rather than through it, as the court found, that their cost is already visible in measles cases, and that whether they stand depends on the appeal. Kennedy has also proposed overhauling the vaccine-injury compensation program, and a 2026 petition asks HHS to add more than 300 conditions to its injury table. The cancelled mRNA contracts left the country less ready for the next pandemic (Module 13).

11d. The Vaccine Business

Vaccine	Company	Disease	2025 sales	Note
Gardasil	Merck	HPV and the cancers it causes	$5.2B, down from $8.6B	Chinese demand collapsed
Prevnar	Pfizer	Pneumococcal disease	$6.5B	Merck's Capvaxive ($759M) competing
Shingrix	GSK	Shingles	£3.6B	Up 8%
Comirnaty; Spikevax	Pfizer and BioNTech; Moderna	COVID	(11b)	Narrower US approvals (11c)
Abrysvo; Arexvy; mRESVIA	Pfizer; GSK; Moderna	RSV in older adults	$1.0B; £0.6B; small	Narrower recommendations
Beyfortus; Enflonsia	Sanofi and AstraZeneca; Merck	RSV in infants (antibodies)	—	Merck's rival approved in June 2025
Childhood vaccines	Merck, Sanofi, GSK, Pfizer	Measles, polio, whooping cough, hepatitis, rotavirus	Not broken out	The schedule in dispute (11c)

Company reports; sales are company claims, and GSK reports in pounds.

The vaccine business is dominated by four companies, Merck, Pfizer, GSK, and Sanofi, and it is unusual: low prices, governments and the vaccine alliance Gavi as buyers, legal shields against liability, and products that prevent rather than treat, which makes vaccines among the most cost-effective medicines ever made and among the least profitable per dose. The trends of 2025-26 run against it: besides the declines in the table, US childhood vaccination slipped, and the policy turn reached manufacturers' forecasts. Outside the United States the problem is money, as Gavi and the WHO lose American funding just as the first malaria vaccines roll out (Module 13).

Module 11 Key Points

Vaccines and mRNA

• The COVID vaccines went from viral sequence to authorization in eleven months and averted an estimated 14-20 million deaths in their first year.

• Poor countries waited: by the end of 2021, fewer than one in ten people in low-income countries had a dose.

• COVID vaccine sales fell by about 90% from their peak; mRNA's first new success is Moderna's 2026 flu vaccine.

• US vaccine policy turned in 2025-26 until a March 2026 court order stayed the new committee and the schedule changes.

• Measles reached 4,080 US cases by October 8, 2026, far above 2025's total and a 35-year high.

Module 11 Quiz

Check Your Understanding

1. What made the COVID vaccines possible in eleven months?

A) A new law
B) Decades of mRNA research, guaranteed purchases, and manufacturing at risk in parallel with trials
C) Skipping the Phase III trials entirely
D) A vaccine bought from China

2. What did the March 2026 court order do?

A) It stayed the January memo and the new committee's appointments and votes.
B) It restored the CDC director to office.
C) It upheld every change.
D) It ordered the FDA to approve all vaccines without review, including those not yet tested in trials.

3. What did the FDA approve for Moderna in August 2026?

A) A COVID pill for children
B) A universal HIV vaccine
C) An mRNA flu vaccine
D) A new measles vaccine

4. Why are vaccines among the least profitable medicines per dose?

A) They are expensive to make.
B) They sell at low prices, often to governments, and prevent rather than treat disease.
C) Their patents are never enforced.
D) They are sold only in poor countries.

5. What happened to Gardasil's sales in 2025?

A) They doubled after the vaccine was added to China's national immunization program for girls
B) They held steady
C) They fell slightly, by about 5%
D) They fell by about 40%

Module 12 — Neuroscience and the Hard Diseases

Where the Industry Has Struggled

Recommended Reading / Reference

Reference: The CLARITY-AD and TRAILBLAZER-ALZ 2 trial publications; the FDA's 2020 advisory-committee transcript on Aduhelm and the 2022 congressional report on its approval; the Alzheimer's Association's *Facts and Figures* (annual); Eisai's and Lilly's 2026 reports; the FDA's 2026 novel-drug approvals

12a. Alzheimer's: Aduhelm and After

Drug or test	Company	What it does	Status	Effect	Price
Aduhelm	Biogen and Eisai	Anti-amyloid antibody	Abandoned (12a)	Disputed (12a)	(12a)
Leqembi	Eisai and Biogen	Anti-amyloid antibody	State of the Art; an injection under the skin for maintenance since August 2025	Slows decline about 27% over 18 months	About $26,500 a year
Kisunla	Eli Lilly	Anti-amyloid antibody	State of the Art	Slows decline about 35% in patients at an early stage	About $32,000 for a year of treatment
Blood tests for p-tau217 and p-tau181	Fujirebio; Roche	Detect Alzheimer's pathology	First FDA clearances in May and October 2025	Replace many PET scans and spinal taps	Hundreds of dollars
Tauklarify	—	A PET tracer that images tau	Approved August 2026	Maps the second hallmark protein	—
Semaglutide	Novo Nordisk	GLP-1 agonist	The evoke trials failed in November 2025	No benefit	—

FDA records, trial publications, and company statements; prices are US list prices.

Aduhelm is the case that set the terms of the Alzheimer's debate. In June 2021 the FDA granted Biogen's antibody accelerated approval because it cleared amyloid plaque from the brain, a surrogate, although its trials had given conflicting evidence on whether patients' thinking improved and the agency's advisory committee had voted ten to none against it, with one uncertain. Three advisers resigned, and Biogen priced the drug at $56,000 a year, then halved the price to $28,200. Medicare limited coverage of such antibodies to patients in approved trials, a 2022 congressional report criticized the closeness of the FDA's work with the company, and in 2024 Biogen abandoned the drug. The lesson is that a surrogate can carry a drug past its own regulator's advisers, and that the final check was the payer rather than the regulator.

The two antibodies that followed were approved on cognitive evidence. Eisai and Biogen's Leqembi and Lilly's Kisunla slow early Alzheimer's decline (table), with brain swelling or bleeding (known as ARIA) in about a fifth of patients and infusions or injections with MRI monitoring. Uptake began slowly but is accelerating: Leqembi sold $555 million in Eisai's fiscal year to March 2026, double the year before, Eisai forecasts about $905 million for the year to March 2027, and 72% of US patients remain on it at 18 months (company claims). Kisunla sold $167 million in the second quarter of 2026. The blood tests may matter more than either drug, because they make diagnosis a routine test rather than a PET scan, and about 7.4 million Americans aged 65 and older have the disease, by the Alzheimer's Association's 2026 estimate, most of

them undiagnosed. Blood tests already supplied about 15% of confirmatory diagnoses in 2025, by Eisai's count.

The deeper dispute is over amyloid itself. Its defenders say that two drugs that remove it now slow the disease, that inherited mutations in the amyloid pathway cause early Alzheimer's, and that a rare protective mutation lowers amyloid and the risk of the disease alike. Its skeptics say that a slowing of about a third, measured on scales where the difference is small for a patient, is a weak return on thirty years, that the drugs carry real risks, and that the field's confidence was inflated by flawed research, including an influential 2006 paper that was retracted in 2024. The evidence supports both in part: amyloid removal works, but modestly, and benefits are largest in the earliest patients. This course's reading is that amyloid is a real but partial cause of the disease, so the next gains will come from treating earlier, with blood tests, and from adding drugs aimed at tau and inflammation, rather than from clearing amyloid faster.

12b. New Mechanisms in Psychiatry and Neurology

Psychiatry went decades without a new mechanism: nearly every antipsychotic since chlorpromazine in the 1950s has blocked dopamine, and most antidepressants since the 1980s act on serotonin. Bristol Myers Squibb's Cobenfy (2024) broke the pattern with a drug for schizophrenia that acts on muscarinic receptors, without the weight gain and sedation of the dopamine drugs, although a 2025 trial adding it to existing treatment failed. Johnson & Johnson's Spravato (esketamine, 2019), Zurzuvae (2023), the first pill for postpartum depression, now owned by Supernus after it bought Sage in 2025, and the psychedelics are the other openings. The FDA rejected MDMA-assisted therapy for PTSD in 2024 on trial-design grounds, and psilocybin for depression is in Phase III. Neuroscience had a productive 2026: Takeda's Orzeyful, the first drug to activate the orexin receptor that keeps the brain awake, for narcolepsy (August), AbbVie's Juvmo for Parkinson's disease (September), Vanda's Bysanti for schizophrenia and bipolar disorder (February), and Otsuka's Simtriyo for ADHD (July). The underlying problem is biology rather than targets: psychiatric diseases have no biomarkers, a third of patients respond to nothing, placebo responses in trials run near 40%, and most large companies left the field in the 2010s.

12c. Pain and Rare Disease

Vertex's suzetrigine (Journavx), approved in January 2025, is the first new mechanism for acute pain in decades: it blocks a sodium channel in pain-sensing nerves, is not an opioid, and does not cause addiction. It sold $50 million in the second quarter of 2026, and its program for chronic pain failed one trial and continues in others; the opioid epidemic (Module 16) is the reason it matters. Rare disease, some 7,000 conditions affecting about 300 million people worldwide, most with no treatment, is where orphan-drug incentives meet prices of $300,000 to several million dollars. Orphan drugs are a large share of new approvals (Module 2), and 2026's include the first treatments for Menkes disease, Alexander disease, and arginase 1 deficiency, as well as Regeneron's gene therapy for an inherited form of deafness. It is a field of scientific triumphs at prices that, multiplied across thousands of diseases, no health system can pay (Module 10).

Module 12 Key Points

Neuroscience and the Hard Diseases

• Aduhelm won accelerated approval in 2021 over its advisers' 10-0 vote against it; Medicare's coverage limits, not the FDA, stopped it.

• Leqembi and Kisunla slow early Alzheimer's by roughly 27-35%, and Eisai forecasts nearly $1 billion of Leqembi sales in fiscal 2026.

• Blood tests cleared in 2025 make Alzheimer's diagnosis routine, opening early treatment for millions of undiagnosed Americans.

• Psychiatry and neurology gained new mechanisms, Cobenfy for schizophrenia and the first orexin agonist for narcolepsy, in fields without biomarkers.

• Suzetrigine is the first non-opioid acute-pain mechanism in decades; rare-disease drugs make up about half of new approvals.

Module 12 Quiz

Check Your Understanding

1. How did the FDA's advisers vote on Aduhelm before its 2021 approval?

A) Ten against, none in favor
B) Unanimously in favor, after the trials showed clear cognitive benefit in every patient group
C) Six to four in favor
D) Eight to two in favor

2. What finally limited Aduhelm's use?

A) The FDA withdrew it within a month.
B) Medicare limited coverage to patients in approved trials.
C) A court banned it in 2022.
D) Biogen gave it away free to every patient, and doctors refused to prescribe it anyway.

3. What did semaglutide's evoke trials find in Alzheimer's disease in 2025?

A) A 50% slowing of decline, the largest effect ever recorded for a drug in the disease
B) A cure
C) A slowing of decline equal to Leqembi's
D) No benefit

4. What was new about Cobenfy?

A) It was the first psychedelic approved by the FDA for depression.
B) It cured schizophrenia outright in its Phase III trials.
C) It acts on muscarinic receptors, not dopamine.
D) It was the first antipsychotic that the FDA ever approved.

5. What is suzetrigine?

A) A non-opioid pain pill
B) An opioid
C) An antibiotic
D) A sleeping pill

Module 13 — Infectious Disease and Global Health

Medicines for the Diseases of the Poor, and Defenses Against the Next Pandemic

Recommended Reading / Reference

Reference: The PURPOSE trial publications (lenacapavir, *New England Journal of Medicine*, 2024-25); WHO, *Global Tuberculosis Report* and *World Malaria Report*; the Global Fund on the lenacapavir rollout (2026); Cavalcanti and colleagues on the aid cuts (*The Lancet*, 2025); the GRAM study of antimicrobial resistance (*The Lancet*, 2024)

13a. HIV, Tuberculosis, and Malaria

Disease	Burden (2024-25)	The medicines	2025-26 developments
HIV	41.0 million living with it; 1.2 million new infections and 570,000 deaths in 2025	Antiretroviral combinations, generic in poor countries at about $45 a year; long-acting injections	Lenacapavir, twice a year (State of the Art), with generics due as early as 2027 (below)
Tuberculosis	10.7 million cases and 1.23 million deaths a year, the deadliest infection	Six-month standard regimens and a four-month option; six-month regimens built on bedaquiline and pretomanid for resistant TB; the century-old BCG vaccine	The M72 vaccine (GSK, with the Gates Foundation's research institute) in Phase III, results due 2027-28
Malaria	282 million cases and 610,000 deaths in 2024, about 95% of the deaths in Africa, mostly children	Artemisinin combinations, with resistance emerging in East Africa; bed nets; seasonal preventive drugs	The first vaccines, RTS,S and the cheaper R21, in more than 20 countries; Novartis's ganaplacide-lumefantrine, a new combination without artemisinin, positive in Phase III (November 2025)
Hepatitis C and B	50 million and 254 million infected	Cures for C in more than 95% of patients; lifelong suppression for B	A functional cure for some patients with B (Module 10); Egypt the first country certified on the path to eliminating C
Neglected tropical diseases	About 1.5 billion people needing treatment	Donated drugs given to whole communities (ivermectin, albendazole)	Sleeping sickness near elimination, treated with a ten-day pill, fexinidazole

UNAIDS, WHO, and company reports; burdens are the latest published figures.

The diseases of the poor kill millions of people a year and receive a fraction of the industry's research, because their patients cannot pay. The drugs that exist came from public funding, philanthropy (the Gates Foundation above all), product-development partnerships such as the Medicines for Malaria Venture, the TB Alliance, and DNDi, and a few companies' tiered pricing and voluntary licenses. Lenacapavir is the model at its best. In the PURPOSE 1 trial not one woman given the injection was infected, Gilead licensed generic makers to supply 120 countries in 2024, and in September 2025 two Indian makers agreed, with backing from the Gates Foundation and Unitaid, to sell it for $40 a year. By April 2026 eight African countries had introduced it and more than 11,000 people had started, and the United States and the Global Fund raised their target to 3 million people through 2028.

13b. The Funding Collapse

Funder	Before 2025	2025-26
USAID	About $40B a year, about $10B of it for health	Dismantled (below); its remaining functions moved to the State Department
PEPFAR, the US HIV program	$6-7B a year; about 20 million people on treatment	Authorization lapsed in March 2025; frozen, partly waived, and cut; now co-funding lenacapavir
The Global Fund (HIV, TB, malaria)	About $5B a year, a third of it from the US	Raised $11.3B against an $18B target in November 2025; the US pledge cut to $4.6B
Gavi, the vaccine alliance	About $2B a year; the US about $300M	The US withheld its pledge in June 2025; raised more than $9B against an $11.9B target
WHO	The US its largest funder	The US withdrawal took effect in January 2026
European donors	Britain, Germany, France, and the Netherlands about $70B a year	Cutting aid to pay for defense; Britain from 0.5% to 0.3% of national income by 2027
Gates Foundation	About $9B a year	Pledged in 2025 to spend $200B and close by 2045; cannot replace governments

Government, OECD, and fund reports; figures are approximate.

The dismantling of USAID in early 2025 removed the world's largest global-health funder within weeks, and PEPFAR, credited with saving 26 million lives, was cut back (table). The administration's case is that aid had become inefficient and open-ended, that other rich countries should pay more, and that targeted bilateral deals, such as its lenacapavir partnership, do more per dollar. Its critics answer that programs were ended before anything replaced them. A 2025 *Lancet* study projected that the USAID cuts alone could cause about 14 million excess deaths by 2030, 4.5 million of them children under five. That figure is a model rather than a count, and the clinic closures and treatment interruptions reported since are consistent with it but do not yet measure it. This course's reading is that the cuts outran any replacement, so large excess mortality is likely even if the projection's size is uncertain, and that the lenacapavir partnership shows targeted US funding continuing inside a much smaller budget.

13c. Antimicrobial Resistance

Resistant bacteria directly killed about 1.14 million people in 2021 and contributed to about 4.7 million deaths, by the GRAM study, which projects 1.9 million direct deaths a year by 2050 and 39 million in total between 2025 and 2050; the widely quoted figure of 10 million a year by 2050 is an older projection from 2014. The cause is use: more antibiotics go to livestock than to people, and over-prescription and poor sanitation do the rest. The market failure is that a new antibiotic must be held in reserve to stay effective, so it sells little. The large companies left the field in the 2010s, small ones such as Achaogen and Melinta went bankrupt after winning approval, and the pipeline is thin. New drugs still arrive, including GSK's gepotidacin, the first of a new class for urinary infections (2025), and two 2026 approvals for complicated urinary infections, among them Utebzi, the first carbapenem in pill form. The fixes, Britain's subscription model, which pays for an antibiotic's availability rather than its volume, the proposed US PASTEUR Act, and the AMR Action Fund's $1 billion, are real but small, and antibiotic candidates found by AI are the science's answer to a problem that is fundamentally economic.

13d. Pandemic Preparedness

The pandemic showed that a vaccine could be made within a year and that the world was not organized to make or share it fairly (Module 11). The response was CEPI's '100 Days Mission' to compress the next vaccine to a hundred days, a WHO pandemic agreement adopted in May 2025 without the United States, and mRNA platforms kept ready. Since then the United States has cancelled its mRNA pandemic contracts (Module 11) and left the WHO, while H5N1 bird flu spread through its dairy herds and infected 70 people, one of whom died, through 2025. The next pathogen, whether H5N1, a new coronavirus, Marburg, or Nipah, will find a world less prepared than in 2022.

Module 13 Key Points

Infectious Disease and Global Health

• Lenacapavir prevented every HIV infection among women in PURPOSE 1, and generics at $40 a year are due as early as 2027.

• Tuberculosis kills about 1.2 million people a year, the most of any infection; the M72 vaccine's Phase III results are due 2027-28.

• USAID's dismantling could cause 14 million excess deaths by 2030, by a 2025 Lancet projection.

• Antimicrobial resistance directly kills over a million people a year, while new antibiotics are held in reserve and sell little.

• Pandemic preparedness has weakened: the US left the WHO and cancelled mRNA contracts as H5N1 spread through dairy herds.

Module 13 Quiz

Check Your Understanding

1. What did lenacapavir achieve in the PURPOSE 1 trial?

A) A 50% cut in infections
B) A cure for HIV in people already infected, confirmed after two years without any treatment
C) No benefit over pills
D) Zero infections among women

2. Which disease is the deadliest infection worldwide?

A) Malaria in Africa
B) HIV infection
C) Tuberculosis
D) Measles in children

3. What did a 2025 Lancet study project from the USAID cuts by 2030?

A) About 1,000 excess deaths
B) 14 million excess deaths
C) No change
D) Higher survival everywhere, as countries replaced American funding with their own budgets

4. Why did large companies leave antibiotic development?

A) A new antibiotic must be held in reserve to stay effective, so it sells little.
B) Regulators banned new antibiotics.
C) Bacteria stopped evolving resistance.
D) Antibiotics became too dangerous to prescribe.

5. When did the US withdrawal from the WHO take effect?

A) In 2020
B) January 2026
C) May 2025
D) December 2026

Module 14 — China's Rise

How China Became the Second Biotech Superpower

Recommended Reading / Reference

Reference: PharmCube and China's drug regulator (NMPA) on out-licensing (2025-26); the National Security Commission on Emerging Biotechnology's final report (April 2025); Stifel and Jefferies reports on Chinese biotech; deal trackers for 2026

14a. The Numbers

Measure	China (2025-26)	Note
Out-licensing to foreign companies	A record $137.7B in 186 deals in 2025; $60B in the first quarter of 2026, up 73%; $100-110B in the first half	Counts differ by tracker; the NMPA gives $135.7B for 2025
Share of global licensing	About a third of licensing spending and a quarter of licensed assets in 2025; about half of headline deal value by some trackers	Spending and asset shares from data presented at the J.P. Morgan Healthcare Conference, January 2026
Upfront payments	About 6% of headline value in the first half of 2026	Headlines overstate the money that changes hands (Module 5)
Deals of $1B or more	27 in 2026 by September 28	
Largest deals	2025: GSK-Hengrui, up to $12.5B. 2026: BMS-Hengrui, up to $15.2B ($600M upfront); Pfizer-Innovent, about $10.5B ($650M upfront); AstraZeneca-CSPC (Module 6); AbbVie-RemeGen, up to $5.6B	Every major Western company has licensed from China
Landmark earlier deals	Summit-Akeso (2022, up to $5B, ivonescimab); Pfizer-3SBio (2025, $1.25B upfront, about $6B in all)	The PD-1/VEGF race (Module 7)
Share of the world's drug candidates	About 30%, by industry estimates	Under a tenth in 2018
Contract manufacturing	WuXi AppTec and WuXi Biologics serve much of Western biotech	The target of BIOSECURE (Module 4)
Regulation	NMPA reforms since 2015: international ICH standards (2017); trials approved by default after 60 working days (2018)	(14b)

PharmCube, NMPA, and press deal trackers; deal values are announced maximums unless stated.

Ten years ago China's pharmaceutical industry made generics and copies of Western biologics. In 2025 it licensed a record value of drug candidates to foreign companies (table), and 2026 is running ahead of that pace. Many of the bispecific antibodies, conjugates, and obesity drugs in Western pipelines are Chinese in origin.

14b. How It Happened

Four things built it. The first was talent: tens of thousands of Chinese scientists trained and worked in American and European pharma in the 2000s and returned, as 'sea turtles', to found companies. The second was regulation, as the NMPA's reforms (table) cleared a years-long backlog. The third was capital: Hong Kong's 2018 rule allowing biotechs without revenue to list, Shanghai's STAR market from 2019, and state funds and provincial governments built the campuses, such as Suzhou's BioBay and Shanghai's Zhangjiang. The fourth was speed and cost. Chinese trials recruit two to three times faster in a hospital

system that concentrates patients, and a candidate reaches Phase II data at an estimated 30-50% of the Western cost, the discount that makes licensing irresistible to a Western company facing a cliff (Module 5). The model is a fast follower becoming an innovator: most Chinese candidates are improved versions of Western mechanisms, engineered faster and more cheaply, and the frontier question is whether they can originate.

14c. The Deal Structures

The deals take three forms. Most are licenses of rights outside China, in which the Chinese company keeps its home market and takes an upfront payment, milestones, and royalties. 'NewCo' structures spin a Chinese asset into a new US company funded by American venture capital, to reduce political risk; Kailera, built on Hengrui's obesity drugs, became the year's benchmark when it went public (Module 3). Outright acquisitions remain rare because both governments review them.

14d. Threat or Solution

Big Pharma regards China as the answer to its patent cliff, a source of cheaper and faster candidates for the years when its own blockbusters lose protection. American biotech companies and national-security voices regard it as a threat: a rival that undercuts the prices Western biotechs need, learns from its Western partners, and answers to a state that Washington now treats as a strategic competitor. Washington's response is divided. BIOSECURE became law (Module 4), the National Security Commission on Emerging Biotechnology called in April 2025 for $15 billion over five years and a national strategy, and the administration's tariffs and pricing deals pull in other directions (Module 17), while cuts to NIH grants and tighter visas weaken the American research base. The evidence so far is that Chinese companies supply much of the licensing (14a) and many of the newest bispecifics and conjugates, but the first test of whether a Chinese drug can displace a Western standard of care, ivonescimab, is unresolved (Module 7). This course's reading is that China has become an indispensable supplier of drug candidates but not yet an originator of standards of care, so the licensing will continue whatever Washington decides, and the policy question is how much of the downstream value, in trials, manufacturing, and launches, stays in the United States.

Module 14 Key Points

China's Rise

• China out-licensed a record $137.7 billion of drug candidates in 186 deals in 2025, and 2026 is running ahead of that pace.

• Chinese companies supplied about a third of global licensing spending in 2025, though upfront payments are only about 6% of headline values.

• Returning scientists, regulatory reform, new capital markets, and fast, cheap trials built the industry within a decade.

• NewCo structures spin Chinese assets into US companies; Kailera, built on Hengrui's obesity drugs, became 2026's benchmark IPO.

• China is now an indispensable supplier of candidates, but whether it can originate standards of care is unproven.

Module 14 Quiz

Check Your Understanding

1. How large was China's drug out-licensing in 2025?

A) It was about $5 billion, in a dozen deals.
B) It was banned by Beijing for national-security reasons.
C) It was $137.7 billion in 186 deals.
D) It was about $500 million, in a handful of deals.

2. What is the 'China discount'?

A) Phase II data at 30-50% of the Western cost
B) A tariff exemption
C) Cheaper generics
D) A currency effect

3. What share of headline value did upfront payments make up in early 2026?

A) Around half
B) All of it, because Chinese law requires the full value of a license to be paid on signing
C) About a quarter
D) Only about 6%

4. What is a 'NewCo' structure?

A) A state-owned exporter
B) A Chinese takeover of a listed US biotech after review by both governments
C) A contract manufacturer
D) A Chinese drug spun into a new US company funded by American venture capital

5. Which company's obesity drugs did Kailera license?

A) Novo Nordisk's
B) WuXi Biologics, which also makes most of the drugs Kailera sells in the United States
C) Hengrui's
D) Eli Lilly's

Module 15 — AI in Drug Discovery

What Artificial Intelligence Has and Has Not Done for Medicine

Recommended Reading / Reference

Reference: The 2024 Nobel Prize in Chemistry citation (Baker, Hassabis, Jumper); Jayatunga and colleagues on the clinical success of AI-discovered molecules (*Drug Discovery Today*, 2024); Insilico Medicine's rentosertib publications; Takeda's 2026 filings on zasocitinib; the FDA's January 2025 draft guidance on AI in drug development

15a. What Changed

DeepMind's AlphaFold (2020-21) solved a fifty-year problem, predicting a protein's three-dimensional shape from its sequence, and made the structures of some 200 million proteins freely available. Demis Hassabis and John Jumper shared the 2024 Nobel Prize in Chemistry for it with David Baker, whose tools design proteins that do not exist in nature, and AlphaFold 3 (State of the Art) extended prediction to how proteins bind drugs, DNA, and one another. Generative models now design candidate molecules and antibodies against a target in hours, language models read the literature and the patents, and machine learning predicts which candidates will be toxic, soluble, or absorbed. The promise is to compress the years of discovery into months and to improve the industry's poor odds of success (Module 2) by picking better targets and molecules.

15b. The Companies and the Deals

Company	Backing	Approach	Status in 2026	Partners
Isomorphic Labs	Alphabet (a DeepMind spinout)	AlphaFold-based design across targets	Raised $600M in 2025 and $2.1B in May 2026; first human trials expected by the end of 2026	Lilly and Novartis (2024, about $2.9B in potential milestones)
Insilico Medicine	Listed in Hong Kong since December 2025	Generative chemistry from target to molecule	Rentosertib in Phase III (State of the Art)	—
Nimbus and Schrödinger	Takeda bought the program for $4B upfront (2022)	Physics-based computational design	Zasocitinib under FDA priority review (State of the Art)	Takeda
Recursion (merged with Exscientia, 2024)	Public	Cell imaging plus generative chemistry	Phase II programs; cut about 20% of staff in 2025	Roche, Sanofi, Bayer
Xaira Therapeutics	More than $1B at its 2024 launch	Protein design from David Baker's lab	Preclinical	—
Generate, Absci, Chai, Latent Labs, Lila	Venture capital	Generative biologics and foundation models	Early clinical or preclinical	Amgen, Novartis, AstraZeneca
Nvidia (BioNeMo), Microsoft, Amazon	Big tech	Computing power and models for drug companies	Infrastructure	Most large drug companies
Big Pharma's own programs	Lilly (TuneLab), Novartis, AstraZeneca, Sanofi	Proprietary models on proprietary data	Every large company has one	Sanofi with OpenAI and Formation Bio

Company announcements and press reports; funding and milestone figures are company claims.

15c. The Honest Scorecard

Claim	Evidence in 2026	Verdict
AI can predict protein structure	AlphaFold; the Nobel Prize	Proven
AI can design molecules and antibodies against a target	Routine; dozens of AI-designed candidates are in trials	Proven for design, not yet for success rates
AI-discovered drugs succeed more often	Phase I success of 80-90%, against about half for drugs overall (Module 2); Phase II success of about 40%, which the study calls comparable to historical averages	Suggestive, on small samples; Phase II is the test
AI has produced an approved drug	Not yet; zasocitinib and rentosertib are the closest (15d)	Not yet
AI cuts discovery from years to months	Insilico: 9-18 months from target to a preclinical candidate and about 30 months to the first human dose (company claims)	Demonstrated in cases
AI cuts the cost per drug	Company claims; no industry-wide evidence	Unproven
AI finds new targets	Genetics and AI have proposed candidate targets, none yet validated by an approved drug	Promising, unproven
AI improves trials	Site selection, patient matching, and monitoring are in use; the FDA issued draft guidance in January 2025	Real and incremental
AI replaces the laboratory	Every candidate still needs synthesis, animals, and patients	No

Jayatunga and colleagues (2024) for success rates; company reports for the rest.

15d. The Verdict So Far

No AI-discovered drug has been approved. The nearest are Takeda's zasocitinib, a psoriasis pill designed with Schrödinger's physics-based software at Nimbus, which counts only if computational design counts as AI, and Insilico's rentosertib for lung fibrosis, now in a Phase III trial of 320 patients (State of the Art). Enthusiasts say that structure prediction and design are proven, that AI-derived candidates pass Phase I far more often, that Isomorphic, Xaira, and the big companies are investing billions, and that the first approval is near (State of the Art). Skeptics say that AI has improved the parts of discovery that are prediction and design and not the part that is biology: whether a target matters in a human, which no model can know until a trial. The evidence fits the skeptics' account of where the gains lie. AI-derived candidates pass Phase I, the safety test, more often, but Phase II, the efficacy test, at the usual rate, which is what one would expect if AI makes better molecules but not better hypotheses. This course's reading is that AI will shorten discovery and modestly raise success rates in the late 2020s without solving the failure of biology in Phase II, and that 'AI-discovered' will soon describe most new drugs and, for that reason, will mean less.

Module 15 Key Points

AI in Drug Discovery

• AlphaFold solved protein-structure prediction and shared the 2024 Chemistry Nobel with David Baker's protein design.

• Isomorphic Labs raised $2.1 billion in May 2026 but had not yet started human trials.

• No AI-discovered drug is approved; zasocitinib, designed by computer, faces an FDA decision in early 2027.

• AI-derived candidates pass Phase I more often but Phase II at the usual rate: better molecules, not better hypotheses.

• Insilico's speed claim is 9-18 months from target to a preclinical candidate, with about 30 months to first human dosing.

Module 15 Quiz

Check Your Understanding

1. What did AlphaFold solve?

A) Protein structure prediction
B) Drug pricing
C) The design of every clinical trial run in the United States since the FDA adopted it in 2023
D) Biologic manufacturing at scale

2. Has an AI-discovered drug been approved as of October 2026?

A) Yes, dozens have been approved.
B) No, though one designed by computer awaits an FDA decision.
C) Yes, AlphaFold's own antibody.
D) No, because the FDA has banned drugs designed with the help of artificial intelligence.

3. What did Isomorphic Labs raise in May 2026?

A) $6 million
B) $2.1 billion
C) About $200 billion
D) Its first $1 billion

4. What do early analyses show for AI-derived drug candidates?

A) They fail more often at every phase.
B) They have not yet entered human trials, so no data exist.
C) They succeed at every phase, including Phase III, without exception across all the programs studied.
D) They pass Phase I more often but Phase II at the usual rate.

5. Which drug, designed by computer, faces an FDA decision in early 2027?

A) Insilico's rentosertib
B) AlphaFold 3, which DeepMind submitted to the FDA as a diagnostic device for protein diseases
C) Zasocitinib
D) Cobenfy's successor

Module 16 — The Regulators

Who Decides What Is a Medicine, and Who Checks Them

Recommended Reading / Reference

Book: Patrick Radden Keefe, *Empire of Pain*

Reference: The Federal Food, Drug, and Cosmetic Act and PDUFA VII; the Food and Drug Omnibus Reform Act (2022); the Vioxx litigation record and the 2004 Senate testimony; Purdue Pharma's 2026 restructuring; Liu, Kesselheim, and Cliff on accelerated approval in cancer (*JAMA*, 2024)

16a. The FDA

Element	Detail
Structure	CDER for drugs, CBER for biologics, vaccines, and gene and cell therapy, and CDRH for devices, plus food, tobacco, and cosmetics; about 18,000 staff before 2025
Funding	About two-thirds of the FDA's budget for human drugs comes from industry user fees (Module 2), under five-year agreements; the current one, PDUFA VII (named for the Prescription Drug User Fee Act), expires on September 30, 2027
Standard	'Substantial evidence' of effectiveness from 'adequate and well-controlled' trials, traditionally two; in 2026 the agency's leaders described a single pivotal trial as the new default
Advisory committees	Outside experts vote, without binding the agency, which usually follows them and occasionally does not (Module 12)
After approval	Adverse-event reporting, risk-management programs, label changes, and withdrawals, which are rare (16c)
Inspections	Domestic and foreign plants; inspections in China and India are a recurring gap

FDA records and press reports.

16b. The 2025-26 Turmoil

The FDA lost about a fifth of its staff in 2025, when HHS announced some 3,500 job cuts on April 1, although some staff were later rehired. Its leadership then turned over. Marty Makary, commissioner from April 2025, promised faster reviews with fewer staff, introduced the national priority vouchers (Module 2) and an AI review assistant called Elsa, and left on May 12, 2026, an exit that reports attributed to Kennedy, with White House approval, after disputes over vaccine trials, approval policy, and the abortion pill mifepristone. Kyle Diamantas, the deputy commissioner for food, is acting commissioner, and no permanent nominee had been named by October 2026. Vinay Prasad, the vaccine center's chief, restricted COVID vaccine approvals (Module 11), attributed at least ten child deaths to COVID vaccines in an internal memo of November 2025 that outside experts disputed, and left for the second time in spring 2026. The drug center, CDER, has had five heads since Patrizia Cavazzoni left in January 2025, one of whom, George Tidmarsh, resigned amid an inquiry into his conduct, and Michael Davis now leads it in an acting capacity.

The administration's case is that the old agency was slow, too close to industry, and too willing to approve drugs on weak surrogates, and that one-trial approvals, priority vouchers, and new pathways for rare diseases (Module 10) bring medicines to patients sooner. Critics answer that the agency has lost the experienced reviewers and stable leadership that make its decisions predictable, and that vaccine decisions have been made for political rather than scientific reasons. The evidence is mixed. Novel approvals fell in 2025 and then recovered their pace in 2026, the priority vouchers have sped drugs through (both Module 2),

and companies report less predictable meetings and decisions. This course's reading is that the FDA has kept approving drugs, faster in places, while losing the continuity on which predictability rests, so the cost shows up less in approval counts than in uncertainty for every company, and the user-fee renegotiation (16a) will show whether the industry still trusts the bargain. Europe's EMA (16d) has had no comparable upheaval.

16c. Safety After Approval: Vioxx and OxyContin

Merck's painkiller Vioxx, approved in 1999 and taken by some 80 million people worldwide, is the defining failure of safety after approval. Its VIGOR trial in 2000 showed more heart attacks than on the older painkiller it was compared with, and Merck explained the gap as that drug's protective effect and kept marketing. In September 2004 another trial confirmed that Vioxx doubled the risk of heart attacks and strokes, and Merck withdrew it. An FDA scientist's estimate put the toll at tens of thousands of deaths, often cited as about 38,000, and Merck settled the lawsuits for $4.85 billion. Congress responded with a 2007 law that gave the FDA power to require safety studies and risk-management programs after approval. The lesson is that safety after approval matters as much as efficacy before it, and that a company that markets past its own data pays for decades.

Purdue Pharma's OxyContin is the larger catastrophe. Launched in 1996, the slow-release opioid was marketed to doctors as carrying little risk of addiction, and prescriptions soared; more than 800,000 Americans have died of opioid overdoses since 1999, most of them later from illicit fentanyl. Purdue pleaded guilty to federal charges in 2007 and again in 2020, and settlements with Purdue, the Sackler family, the distributors McKesson, Cardinal, and Cencora (about $21 billion together), pharmacies, and Johnson & Johnson now exceed $50 billion. Purdue's bankruptcy plan, confirmed in November 2025, took effect on May 1, 2026: about $7.4 billion in cash goes to creditors, most of it from the Sacklers, who contribute up to $6.5-7 billion, individual victims receive up to $865 million, and the business passed to Knoa Pharma, owned by a foundation in which the Sacklers have no role. The lesson is that marketing can create an epidemic, and that every link in the chain, from maker to distributor to pharmacy, shared both the profits and the liability. A painkiller with a new, non-opioid mechanism arrived only recently (Module 12).

16d. The Other Regulators

Regulator	Jurisdiction	Character
EMA (European Medicines Agency)	The EU's 27 countries, through one centralized approval	Scientific and consensus-based, slower on average, with conditional approvals; prices are set nationally afterward (Module 17)
NMPA	China	Transformed by reform (Module 14)
PMDA	Japan	Rigorous; its 'drug lag' behind the US is shrinking; often requires Japanese trial data
MHRA	Britain	Faster since Brexit, often relying on FDA and EMA decisions
Health Canada, Australia's TGA, Brazil's ANVISA, India's CDSCO	National	Increasingly rely on FDA and EMA reference approvals
WHO prequalification	Purchases by Gavi, UNICEF, and the Global Fund	The gatekeeper for vaccines and generics in poor countries
ICH (International Council for Harmonisation)	The US, EU, Japan, China, and others	Common technical standards, so that one trial package can serve every market

Agency publications.

16e. Surrogates and Accelerated Approval

A drug is judged by its trial's endpoint. The gold standard is a hard outcome, such as death, a heart attack, or a cure, measured in a randomized, double-blind trial against placebo or standard care. Many modern approvals rest instead on surrogates: tumor shrinkage or progression-free survival rather than overall survival, LDL cholesterol rather than heart attacks, HbA1c, a measure of blood sugar, rather than the complications of diabetes, or amyloid rather than cognition. Accelerated approval, which allows a surrogate 'reasonably likely' to predict benefit (Module 2), is where the debate is sharpest. Its defenders say it brings drugs to patients with fatal diseases years earlier and that failed drugs can be withdrawn. Its critics say confirmatory trials run late or fail while patients take, and payers fund, drugs of unproven value, as with Aduhelm (Module 12) and Elevidys (Module 10). The evidence supports the critics' concern: a 2024 *JAMA* study found that fewer than half of the cancer drugs given accelerated approval in 2013-17 had shown a clinical benefit in confirmatory trials more than five years later. A 2022 law, the Food and Drug Omnibus Reform Act, let the FDA require confirmatory trials to be under way at approval and withdraw failures faster. This course's reading is that accelerated approval is worth keeping for fatal diseases without alternatives, but only with those trials running at approval and with labels narrowed or withdrawn quickly when they fail, which is the standard that Elevidys tested. Trials are also where the industry's costs (Module 2) and its inequities lie: they enroll few Black and Hispanic patients, and they increasingly run in China for speed.

Module 16 Key Points

The Regulators

• FDA user fees fund about two-thirds of its drug budget, and the PDUFA agreement that sets them expires in September 2027.

• The FDA lost about a fifth of its staff in 2025, and its commissioner, vaccine chief, and drug-center head all left by May 2026.

• Vioxx doubled heart risk and was withdrawn in 2004 after Merck explained away its own trial's warning; it cost $4.85 billion.

• OxyContin's marketing helped start an opioid epidemic; Purdue's bankruptcy plan, effective May 2026, moved its business to a foundation-owned successor.

• Accelerated approval speeds drugs to dying patients, but fewer than half of cancer drugs approved that way in 2013-17 later proved a clinical benefit.

Module 16 Quiz

Check Your Understanding

1. How is about two-thirds of the FDA's drug budget funded?

A) By user fees that drug companies pay with each application
B) By patients
C) By foreign governments
D) By a tax on all prescriptions sold in pharmacies

2. Who was acting FDA commissioner after Marty Makary left in May 2026?

A) Vinay Prasad, who returned to run the whole agency after leaving CBER twice
B) Robert Califf
C) Kyle Diamantas
D) Mehmet Oz

3. Why was Vioxx withdrawn in 2004?

A) It failed to relieve pain
B) A trial confirmed that it doubled the risk of heart attacks and strokes, a signal Merck had explained away since 2000
C) Its patent expired
D) It was found to cause liver failure in a large share of the patients who took it daily

4. What company now runs Purdue Pharma's former business?

A) Pfizer
B) The Sackler family
C) Teva Pharmaceuticals
D) Knoa Pharma

5. What did a 2024 study find about cancer drugs given accelerated approval in 2013-17?

A) Under half showed clinical benefit
B) Every one of them was later confirmed to extend patients' lives in large randomized trials
C) All were withdrawn within a year of approval
D) Most cured the cancers they were approved for

Module 17 — Pricing, Policy, and Access

The Pricing Wars of 2025-26, and the Global Access Question

Recommended Reading / Reference

Reference: RAND, *International Prescription Drug Price Comparisons* (2024); CMS on the Medicare Drug Price Negotiation Program (2026-27 cycles); the April 2026 Section 232 proclamation on pharmaceuticals; the UK-US medicines agreement (December 2025); the EU pharmaceutical package (2026 texts)

17a. Why the US Pays More

The United States is the industry's largest and most profitable market (Module 1) because it has no national price regulation: manufacturers set list prices, insurers and PBMs negotiate rebates (Module 4), and Medicare was barred from negotiating until a 2022 law. RAND estimated in 2024 that US prices for brand-name drugs were more than three times those of other rich countries even after estimated rebates, while US generics were cheaper than elsewhere. Europe's systems negotiate nationally, use cost-effectiveness thresholds, reference one another's prices, and refuse drugs that fail the test. Britain's NICE, the standard example, raised its threshold to £25,000-35,000 per quality-adjusted life year under the UK-US deal of December 2025. The deal also capped Britain's rebate on newer medicines at 15% for 2026-28, kept a 0% US tariff on British medicines for three years, and committed Britain to double its spending on new medicines as a share of GDP over ten years. The price of Europe's discipline is later access and an industry that treats Europe as a secondary market. The American argument is that its prices fund the world's innovation, and the European reply is that America overpays for it; both are partly true.

17b. The Instruments of 2025-26

Instrument	What it does	Status (October 2026)
Medicare negotiation (Inflation Reduction Act)	CMS negotiates prices for the drugs on which Medicare spends most: 10 for 2026, 15 for 2027, 15 for 2028, and up to 20 a year after	The first ten, including Eliquis, Jardiance, and Farxiga, in effect since January 1, 2026 at 38-79% below list. All 15 for 2027 are agreed, including semaglutide at $274 a month, and by CMS's estimate the 15 prices would have cut net spending by about 36%; the third list, the first with physician-given drugs such as Botox and Cosentyx, has prices due by November 30, 2026
Medicare Part D redesign	An annual cap on patients' costs and a monthly cap on insulin (17d)	The cap was $2,000 in 2025 and is $2,100 in 2026
Most-favored-nation deals	Companies give Medicaid the lowest price among rich countries, launch new drugs at that price, and sell some drugs for cash through TrumpRx.gov, in return for tariff relief	All 17 companies that received letters in July 2025 signed, and nine more joined on August 31, 2026, making 26 and, by the administration's count, 89% of the branded market; TrumpRx live since February 5, 2026; the obesity-drug terms in Module 6
Section 232 tariffs	100% on patented drugs and their ingredients; 20% for companies with approved plans to build US plants, rising to 100% in April 2030; 0% for companies with both a plant plan and a pricing deal until January 20, 2029	Proclaimed April 2, 2026; in force for 17 large companies on July 31 and for everyone else on September 29, 2026; caps of 15% for the EU, Japan, South Korea, and Switzerland, with Britain's rate in 17a; generics and biosimilars exempt

Instrument	What it does	Status (October 2026)
PBM reform	Delinks PBM pay from list prices and passes rebates through	Law (Module 4)
340B	Hospitals and clinics serving poor patients buy drugs at deep discounts	About $81B of purchases in 2024; manufacturers' rebate models in litigation
Importation	States buy drugs from Canada	Florida's program, approved in 2024, has negligible volume

CMS, the White House, the April 2026 proclamation, and press reports; savings and market shares are government claims.

17c. The Pricing War, Contested

The administration's case is that leverage worked. Under threat of tariffs, companies signed the deals in the table, and the White House counts about $400 billion of US investment pledged. The British deal shows that what it calls foreign freeloading can be renegotiated. Its critics say that the deals are confidential and voluntary and do not touch the list prices of existing drugs: at least 350 US list prices rose on January 1, 2026, including at least five deal-signers, among them about 80 of Pfizer's drugs. Medicaid already received the deepest rebates, cash prices help mainly the uninsured, and the tariffs, after their exemptions and caps, are leverage rather than revenue, falling mainly on smaller companies without deals. Supporters of Medicare negotiation point to its statutory discounts (table). The industry answers that the 'pill penalty', which exposes small molecules to negotiation four years earlier than biologics, distorts research toward biologics, and Congress widened the exemption for orphan drugs in July 2025. The evidence so far is thin: no independent accounting of the deals' net savings has been published, the first year of negotiated prices has not been evaluated, and the tariffs have had no visible effect on prices, which forecasters expect to rise by about 3.5% in 2027. This course's reading is that Medicare negotiation is the instrument with measurable, statutory savings, while the deals and tariffs have produced commitments and leverage rather than measured savings, so the pricing war's results are real for Medicare and Medicaid and unproven for everyone else.

17d. Insulin: The Case That Explains the System

Insulin was discovered in 1921, and its discoverers sold the patent to the University of Toronto for $1 each so that it would be cheap. By 2019 the US list price of a vial of Lilly's Humalog had reached about $275, as the three makers, Lilly, Novo, and Sanofi, raised list prices in step while their net prices stayed flat or fell. Patients without insurance, who paid list prices, rationed it, and some died. The cause was the rebate system: list prices rose to fund rebates to the PBMs, which were paid in part as a share of the list price (Module 4). The responses came together in 2022-24: the Inflation Reduction Act capped Medicare patients' insulin costs at $35 a month, the three makers cut list prices by up to 70% in 2023, California contracted to make its own insulin, and the FTC sued the largest PBMs over insulin rebates in 2024, a case they have largely settled (Module 4). The lesson is that a drug can cost little to make and a great deal to buy when the middlemen are paid on the list price.

17e. Europe and the Rest

Europe's model of national negotiation and refusal is under strain from both sides. The American deals push manufacturers to raise European prices or delay launches, and the EU's pharmaceutical package, whose final texts were published in March 2026 and which is due for formal adoption in autumn 2026, trades

shorter protection for access. It cuts baseline protection from eight years of data protection and two of market protection to eight and one, with extensions for companies that run comparative trials or launch across the EU, and companies can lose exclusivity in a member state if they ignore its request for a launch for three years; most provisions will apply from about 2028. Japan now revises drug prices every year, China's national reimbursement list wins average price cuts of about 60% in return for inclusion, and India controls prices and has licensed generic copies of patented drugs in some cases. The poorest countries depend on voluntary licenses, the Medicines Patent Pool, and donor purchases, the system through which lenacapavir's generics (Module 13) will arrive.

17f. The Access Question

About two billion people lack access to essential medicines, and the reasons are price (a $2 million gene therapy or a $100,000 cancer drug), infrastructure (no transplant center, no cold chain), and money (Module 13). The industry's tools, tiered pricing, voluntary licenses, patent pools, and donation programs, have worked for HIV, hepatitis C, and malaria and not for cancer, biologics, or the new modalities, whose prices are set by American willingness to pay and whose manufacturing is hard to copy. The pricing war is an American argument about American prices. The access question is whether the medicines of Modules 6-12 reach the nearly 8 billion people outside the United States within their patent lives, and the record says that some do, slowly, and the rest arrive with generics.

Module 17 Key Points

Pricing, Policy, and Access

• US brand-name drug prices run about three times other rich countries' after rebates, while US generics are cheaper, by RAND's 2024 estimate.

• Medicare's first ten negotiated prices took effect in January 2026 at 38-79% below list; fifteen more, including semaglutide, follow in 2027.

• Twenty-six companies signed most-favored-nation deals, but the deals do not cut existing list prices, and January 2026 brought 350-plus increases.

• Section 232 tariffs reach 100% on patented drugs, with 0% for companies that have onshoring plans and pricing deals until 2029.

• Insulin's discoverers sold its patent for $1; its US list price reached about $275 a vial before caps and 2023's cuts.

Module 17 Quiz

Check Your Understanding

1. Why do US brand-name drugs cost more than elsewhere?

A) Higher taxes
B) Longer patents
C) Costlier factories
D) No national price regulation

2. What took effect on January 1, 2026?

A) A federal ban on all rebates paid to the PBMs.
B) Free insulin for every diabetic patient in America.
C) Medicare's first negotiated prices did.
D) A national cap on the price of every branded drug.

3. How many companies had signed most-favored-nation deals by September 2026?

A) Three
B) Twenty-six
C) Seventeen
D) Over a hundred

4. What does TrumpRx sell?

A) Drugs at cash prices
B) Insurance
C) Medicare supplement plans
D) Shares in drug companies

5. Why did insulin's US list price rise while its net price stayed flat?

A) List prices rose to fund rebates to PBMs
B) Insulin became costlier to make
C) The FDA required new trials of every insulin before each price increase could take effect
D) Patent extensions blocked all competition for decades

Module 18 — Devices and Diagnostics

The Other Half of Medical Technology

Recommended Reading / Reference

Book: John Carreyrou, *Bad Blood*

Reference: 2025-26 reports from Medtronic, Abbott, Stryker, Boston Scientific, and Intuitive Surgical; Grail's NHS-Galleri results (ASCO, 2026); the FDA's list of AI-enabled devices; the EU Medical Device Regulation

18a. The Industry

Company	Country	Revenue (latest year)	Main businesses	Note
Medtronic	US (domiciled in Ireland)	$36.4B (year to April 2026)	Heart devices, surgery, neuroscience, diabetes	Its diabetes unit, MiniMed, went public in March 2026 ahead of a full separation
Johnson & Johnson MedTech	US	$31.9B (2024)	Orthopedics, surgery, vision, heart (Shockwave, Abiomed)	About a third of J&J's revenue
Abbott	US	$44.3B, of which devices $21.4B (2025)	Glucose monitors (diabetes care $8.0B), heart devices, diagnostics	Bought Exact Sciences, maker of the Cologuard test, for about $21B (agreed November 2025, closed March 2026)
Stryker	US	$25.1B (2025)	Orthopedic implants, the Mako robot, hospital equipment	The leader in orthopedics
Boston Scientific	US	$20.1B (2025), up 20%	Heart devices (Watchman, Farapulse ablation)	The fastest-growing large company
Intuitive Surgical	US	$10.1B (2025), up 21%	Robotic surgery (da Vinci)	About 3.15 million procedures in 2025, up 18%
Siemens Healthineers	Germany	About €23B	Imaging (MRI, CT), diagnostics, radiotherapy (Varian)	The leader in imaging
GE HealthCare, Philips, Roche Diagnostics, Danaher	US, Netherlands, Switzerland	$10-20B each	Imaging; diagnostic instruments and tests	Philips's sleep-apnea recall; Roche's strength in laboratories
Dexcom, Insulet, Edwards, Zimmer Biomet, BD	US	Several billion dollars each	Glucose monitors, insulin pumps, heart valves, orthopedics, syringes	Over-the-counter monitors (18b)
Mindray, United Imaging	China	About $1-5B each	Monitors, consumables, imaging	Favored at home by 'buy Chinese' procurement rules

Company reports; revenue figures are company claims, and the Siemens figure is approximate.

Medical devices, from syringes and stents to MRI scanners and surgical robots, are an industry of roughly $600 billion a year, about a third the size of pharma, with steadier growth, shorter product cycles, and less pricing controversy, because devices are bought by hospitals and priced into procedures rather than listed on a formulary. The leaders are American, with German and Dutch strength in imaging and fast-rising Chinese makers, and their exposure to the obesity drugs (Module 6) is the industry's new uncertainty.

18b. The Technologies

Technology	What it does	Leaders	Scale and frontier
Continuous glucose monitors	A sensor under the skin reads glucose every few minutes and sends it to a phone	Abbott (FreeStyle Libre), Dexcom	More than 10 million users; over-the-counter versions for people without diabetes since 2024
Insulin pumps and closed loops	Pumps that dose insulin from the monitor's readings, an 'artificial pancreas'	Insulet (Omnipod), Tandem, Medtronic	Standard for type 1 diabetes; fully automated systems next
Robotic surgery	A surgeon controls instruments from a console	Intuitive (more than 10,000 da Vinci systems), Medtronic (Hugo), Stryker (Mako), Johnson & Johnson (Ottava)	870 da Vinci 5 systems placed in 2025 (State of the Art); smaller, cheaper systems next
Heart devices	Stents, valves replaced through a catheter (TAVR), leadless pacemakers, pulsed-field ablation, closure of the heart's left atrial appendage	Edwards, Medtronic, Boston Scientific, Abbott	TAVR has replaced open-heart surgery for most valve patients; devices for hypertension and heart failure next
Neuromodulation and brain-computer interfaces	Implants that stimulate nerves or read brain signals	Medtronic (deep-brain stimulation); Neuralink, Synchron, Precision Neuroscience	No brain-computer interface has full FDA approval; Precision has clearance for temporary use of up to 30 days (2025); Neuralink had implanted about a dozen people by September 2025
Imaging and AI	MRI, CT, and ultrasound, increasingly read with AI	Siemens, GE, Philips; Butterfly (handheld ultrasound)	More than 1,200 AI-enabled devices on the FDA's list by mid-2025, mostly in radiology
Implants and orthopedics	Hips, knees, and spine	Stryker, Zimmer Biomet, J&J DePuy, Smith+Nephew	More than a million US joint replacements a year; robotic placement
Wearables	Watches, rings, and remote monitoring	Apple, Samsung, Oura, Whoop	FDA-cleared detection of irregular heart rhythm and sleep apnea on watches

Company reports and FDA records.

18c. Diagnostics

Diagnostics, the tests that decide who gets which drug, are the faster-changing half. Liquid biopsy detects tumor DNA in blood, both to choose treatments (Guardant, Foundation Medicine) and to screen; the first Alzheimer's blood tests have been cleared (Module 12); sequencing a genome now costs under $200, by Illumina's and China's MGI's claims, which makes the diagnosis of rare diseases routine; and molecular and point-of-care tests reach clinics and homes. The industry's cautionary tale is Theranos, valued at $9 billion for a blood-testing device that never worked, exposed by journalism in 2015 and ended by fraud convictions in 2022. Its lesson, that a test's claims must be validated as rigorously as a drug's, was the FDA's argument for regulating tests developed by laboratories, a 2024 rule that a federal court struck down in March 2025.

The largest test of screening was Grail's Galleri, a blood test that looks for signals of more than 50 cancers. Its British trial, NHS-Galleri, enrolled 142,250 people aged 50-77 for three annual rounds and reported in May 2026. It missed its primary goal, a reduction in cancers found at stages III and IV, although stage IV diagnoses fell by 14% in a secondary analysis of only nominal significance; about half of positive results proved to be cancer (company claims). Supporters say the test finds cancers, such as pancreatic and

ovarian, for which no screening exists, and that fewer stage IV diagnoses should mean fewer deaths. Skeptics say the trial was designed to show a fall in late-stage cancers and did not, that no evidence yet shows lives saved, and that false positives and follow-up scans carry costs. This course's reading is that Galleri finds cancers but has not shown that finding them earlier saves lives, so population screening should wait for evidence on deaths.

18d. The Regulatory Divide

Devices are regulated more lightly than drugs. In the United States, the 510(k) pathway clears most devices as 'substantially equivalent' to an existing one, without clinical trials, the route through which faulty hip implants, surgical mesh, and Philips's sleep-apnea machines reached patients, while high-risk devices need premarket approval with trials. Europe's Medical Device Regulation, applied from 2021, tightened the rules so far that companies complained of a backlog and withdrew products, and the EU extended its deadlines into 2027-28. The industry's other structural fact is that its innovation is engineering rather than biology, so its failure rates are lower.

Module 18 Key Points

Devices and Diagnostics

• Medical devices are a roughly $600 billion industry, about a third the size of pharma, priced into procedures rather than formularies.

• Intuitive's da Vinci robots performed about 3.15 million procedures in 2025, up 18%, as Medtronic's Hugo entered the US.

• Galleri's NHS trial missed its main goal of fewer late-stage cancers in 2026, though stage IV diagnoses fell 14%.

• Most US devices are cleared as 'substantially equivalent' to existing ones, without trials, a route that let faulty hips and mesh through.

• No brain-computer interface has full FDA approval; Neuralink had implanted about a dozen people by September 2025.

Module 18 Quiz

Check Your Understanding

1. How do device prices mainly reach payers?

A) Via formularies
B) Via tariffs
C) Priced into hospital procedures
D) Via direct sales

2. How many da Vinci procedures were performed in 2025?

A) About 300,000
B) About 30 million
C) About 31.5 million worldwide
D) About 3.15 million

3. What did the NHS-Galleri trial find?

A) A 50% cut in cancer deaths among the 142,250 people screened over three years
B) It missed its primary goal
C) That the test found no cancers at all
D) A large fall in stage III and IV cancers combined

4. What is the 510(k) pathway?

A) A pricing rule
B) A requirement that every device pass two randomized trials before it can be sold in the US
C) Clearance by equivalence, without trials
D) The European rule that replaced the CE mark in 2021 for every device

5. What regulatory status had brain-computer interfaces reached by October 2026?

A) Full approval for Neuralink's implant in 2025
B) Trials and a 30-day clearance
C) Approval for home use by paralyzed patients across Europe and the United States
D) A federal ban on human implants

Module 19 — Where Things Stand, and What to Watch

The Argument, the Contradictions, and the Signals Ahead

Recommended Reading / Reference

Reference: IQVIA Institute, *Global Use of Medicines* (annual); Evaluate, *World Preview* (annual); the National Security Commission on Emerging Biotechnology's final report (2025); CMS and FDA calendars for 2026-28

19a. The Argument

Five forces are reshaping the industry at once. Obesity has become what statins were, a mass-market chronic therapy, now arriving as pills, monthly injections, and generics, with prices falling as fast as volumes rise (Module 6). China has become a supplier of drug candidates that the industry cannot do without, and its first test as an originator is under way (Modules 7 and 14). AI has arrived in the design of molecules but not in the biology that decides Phase II (Module 15). The largest patent cliff in the industry's history (Module 5) has met price negotiation, pricing deals, tariffs, and PBM reform at the same moment (Modules 4 and 17). And the modalities keep multiplying, from gene editing and RNA drugs to cell therapies, conjugates, and bispecifics, with cures that work and business models that often do not (Module 10). Around all five, the American institutions that built the modern industry, its regulator, its vaccine system, its research funding, and its global-health programs, are under more strain than at any time in a generation (Modules 11, 13, and 16).

19b. Who Checks the Industry

The cases in this course share a lesson: the industry's turning points have been about evidence and incentives rather than molecules. Vioxx and OxyContin were companies marketing past their own data (Module 16), and insulin was a pricing system paid on the list price (Module 17). Humira was a legal strategy that delayed a cliff (Module 5), and the CRISPR babies were a technology that outran its rules (Module 10). Elevidys and Aduhelm were regulators accepting surrogates for diseases with no alternatives (Modules 10 and 12), and the COVID vaccines showed what the same system can do when it is aimed at one goal (Module 11). The corollary is that the checks that worked were often not the regulator's: Medicare's coverage limits stopped Aduhelm, litigation made the opioid makers and distributors pay, journalism exposed Theranos, scientists condemned He Jiankui, and payers and courts have done much to set prices. With the FDA's top posts filled on an acting basis and its vaccine decisions in court, who checks the industry is a more open question than at any time since Vioxx.

19c. The Contradictions

Tension	One side	The other
Innovation and price (Module 17)	American prices, the highest among rich countries, fund much of the world's drug innovation	The US now sets some drug prices, while list prices on existing drugs keep rising
China as solution and threat (Module 14)	Big Pharma fills its cliff years with Chinese candidates at a discount	American biotech loses pricing power, and Washington restricts Chinese suppliers as licensing grows
Speed and evidence (Module 16)	Accelerated approval brings drugs to dying patients years early	Aduhelm, Elevidys, and withdrawn cancer drugs show what surrogates miss
Cures and business models (Module 10)	Gene therapy and editing cure diseases in one treatment	A cure sells only once, and much of the field's pioneering generation has failed commercially
Vaccines' triumph and rejection (Module 11)	mRNA vaccines arrived within a year of the pandemic's start, and the platform now makes a flu vaccine	The US government dismantled its vaccine advisory system until a court stopped it
Science and money in global health (Module 13)	Twice-yearly HIV prevention, malaria vaccines, and a TB vaccine in Phase III	The largest donor cut its aid faster than anything could replace it
The FDA's promise and its capacity (Module 16)	Faster reviews, one-trial approvals, and priority vouchers	Its staff cut and its top posts held by acting officials

Each side is argued in the module named in its row's subject.

19d. What to Watch

Date	Signal	Why it matters
November 3, 2026	US midterm elections	Congress oversees drug pricing, the FDA's user-fee renewal, and the restrictions on Chinese suppliers
Fourth quarter of 2026	CVC and GBL's €10.7B purchase of Recordati expected to close	Private equity's appetite for mid-size drug companies
Early 2027	Sun Pharma's purchase of Organon (Module 5) expected to close	An Indian generic maker buying a Western company
By February 1, 2027	CMS selects the drugs for the fourth round of Medicare negotiation (Module 17)	Whether negotiation keeps expanding
First half of 2027	Intellia's planned US launch of lonvo-z (company plan)	The first CRISPR medicine that edits genes inside the body
By April 2027	The Commerce Department's report on whether to tariff generic drugs	Generics fill most US prescriptions at the lowest margins
Late 2027 at the earliest	Rentosertib's Phase III result, from a 52-week trial (Module 15)	The first full test of an AI-discovered drug
November 7, 2028	US presidential election	The pricing deals and tariffs rest on executive action
No date	Permanent heads for the FDA and its drug and biologics centers	The agency's predictability
No date	The appeals court's ruling on the stay of the vaccine changes	The childhood vaccine schedule

Company plans, agency calendars, and statutory deadlines; items dated in earlier modules are not repeated here.

19e. The Last Word

A decade ago the industry's question was whether it could still invent, and it has answered: obesity, sickle-cell disease, HIV prevention, and a dozen cancers now have treatments that did not exist in 2016. The question it leaves for the next decade is institutional. The same months that brought obesity pills and an editor that works inside the body also brought an FDA run by acting officials, a vaccine schedule decided in court, a fight over prices conducted through tariffs, and an aid system cut faster than it could be replaced. Science sets what is possible and institutions set what is delivered, and in 2026, for the first time in a generation, the second is the harder problem.

Module 19 Key Points

Where Things Stand, and What to Watch

• Obesity drugs, Chinese candidates, AI design, and new modalities are reshaping the industry as its largest cliff meets new price controls.

• The cases share a lesson: turning points come from evidence and incentives, and the checks that worked were often not the regulator's.

• The decade's contradictions pit innovation against price, speed against evidence, and cures against business models.

• Watch the 2026 midterms, the fourth negotiation list due by February 2027, and lonvo-z's planned launch in 2027.

• Science now sets what is possible; institutions, from the FDA to aid budgets, set what reaches patients.

Module 19 Quiz

Check Your Understanding

1. Which check stopped Aduhelm?

A) A federal court order that banned all sales of anti-amyloid antibodies in 2022
B) Biogen's board
C) Medicare's coverage limits
D) The FDA's own advisory committee, whose vote bound the agency

2. What now limits medicine more than science does?

A) Its institutions
B) A shortage of new drug targets, as genetics has run out of leads
C) The cost of computing power
D) Patents that last too long in every market

3. By when must CMS select the fourth round of drugs for Medicare negotiation?

A) By 2035
B) Only after Congress votes to renew the program, which expires at the end of 2026
C) By February 1, 2027
D) By December 31, 2029

4. What lesson do the course's cases share?

A) Molecules alone decided every turning point.
B) Turning points came from evidence and incentives, and the checks that worked were often not the regulator's.
C) Regulators caught every failure early.
D) Companies always disclosed their own trial data in full.

5. Which planned 2027 launch would be the first in-body CRISPR medicine?

A) Casgevy
B) Zolgensma, after Novartis converted it into a gene editor in a 2025 reformulation
C) Leqvio
D) Intellia's lonvo-z

Answer Sheet

Answers to every module's Check Your Understanding quiz.

Module	Answers
Module 1 Quiz	1. D 2. B 3. C 4. A 5. D
Module 2 Quiz	1. B 2. C 3. A 4. B 5. A
Module 3 Quiz	1. C 2. D 3. C 4. D 5. B
Module 4 Quiz	1. A 2. C 3. A 4. B 5. D
Module 5 Quiz	1. A 2. C 3. D 4. B 5. A
Module 6 Quiz	1. B 2. C 3. D 4. D 5. B
Module 7 Quiz	1. A 2. C 3. D 4. C 5. B
Module 8 Quiz	1. A 2. D 3. B 4. C 5. A
Module 9 Quiz	1. D 2. B 3. C 4. A 5. A
Module 10 Quiz	1. D 2. B 3. C 4. D 5. C
Module 11 Quiz	1. B 2. A 3. C 4. B 5. D
Module 12 Quiz	1. A 2. B 3. D 4. C 5. A
Module 13 Quiz	1. D 2. C 3. B 4. A 5. B
Module 14 Quiz	1. C 2. A 3. D 4. D 5. C
Module 15 Quiz	1. A 2. B 3. B 4. D 5. C
Module 16 Quiz	1. A 2. C 3. B 4. D 5. A
Module 17 Quiz	1. D 2. C 3. B 4. A 5. A
Module 18 Quiz	1. C 2. D 3. B 4. C 5. B
Module 19 Quiz	1. C 2. A 3. C 4. B 5. D