China Pulse

Trends in The Changing Pharmaceutical Landscape in China

September 2024

Chinese pharmaceutical innovation has come of age and is feeding the global drug pipeline; domestic market is witnessing growth of private insurance and online pharmacies

R&D

Case 1:

Brukinsa and Carvykti have put the “made in China” innovation model on the world stage; China is now a hotbed for global BD deal sourcing

Case 2:

50% of the ADC pipeline is made in China; while global trials are needed, many of these ADCs are at the cutting edge of innovation

Case 3:

Chinese biotechs are among the global leaders in CAR-T innovation, including universal CAR-T

Case 4:

Chinese biotechs are also scaling up innovation in autoimmune and endocrine diseases, including GLP-1R targeted obesity drugs

Regulatory

Case 5:

China is streamlining its accelerated approval pathways for high unmet needs drugs

Payers

Case 6:

Orphan drugs still face patient access challenges, but regulatory and reimbursement reforms are creating a more favourable environment

Case 7:

Led by RCCMI programs, private medical insurances are rapidly growing across China

Commercial

Case 8:

Ultra-low prices and poor quality stemming from VBP have inadvertently boosted market demand for high-end expensive products

Case 9:

Online medical platform and DTP pharmacies are quickly developing and have become a significant drug sales channel in recent years

Ecosystem

Case 10:

Overall healthcare environment is evolving to be more product-centric and market-driven in China

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Note: RCCMI – regional customized commercial medical insurance; VBP – value-based purchasing; DTP - direct to patient

The "Made-in China" pharmaceutical innovation model has been proven in the last few years

Chinese Innovative Medicines Approved in the US/EU:

Chinese Originator	Global Partner	Drug	US/EU Indications*	FDA Approval Date	Deal Value	2023 Sales
Beigene	--	Brukinsa® zanubrutinib 80mg capsules	CLL/SLL, WM, MCL, MZL, FL	Nov. 2019	N/A	*$946M (US)* *$1,290M (Worldwide)* *[$2B+ expected in 2024]*
Legend	J&J	CARVYKTI® (ciltacabtagene autoleucel)	MM	Feb. 2022	*Global License: $1,700M upfront /milestone + 50/50 profit/cost sharing ex-China + 70/30 profit/cost sharing in China*	*$470M (US)* *$500M (WW)*
TopAlliance	Coherus	LOQTORZI® (toripalimab-tpzi) injection	NPC	Oct. 2023	US and Canada rights: *$290M upfront/milestone + 18% of net revenue*	*$0.6M (US)*** *$130M (WW)*
HutchMed	Takeda	Fruzaqla® (fruquintinib) capsules	mCRC	Nov. 2023	Global exclusive rights (ex. China)*: $1,130M upfront/milestone*	*$5M (US)* *$197M (WW)****
Beigene	Novartis (Returned to BeiGene)	TEVIMBRA (tislelizumab)	ESCC	Mar. 2024	Ex-China rights: *$1,550M milestone and tiered % on revenue;* Ended partnership in 2023	*none (US)* *$537M (WW)*

Brukinsa and Carvykti have demonstrated their differentiation and strong adoption in the U.S. market

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Note: *the listed indications are up-to-date as of Jul. 2024; ** Loqtorzi is only launched in US in December 2023; *** the revenue of Fruzaqla is for the fiscal year of Apr 2023 – Mar 2024;

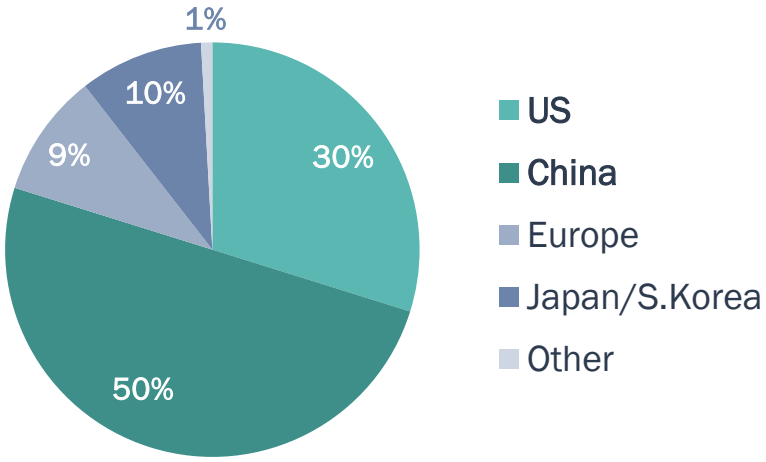
Half of global ADCs originated in China; these Chinese ADCs are being developed for tumor types both universally prevalent and locally endemic

R&D

50% of the ADCs in the world are created in China

Clinical stage ADCs worldwide (N=110)

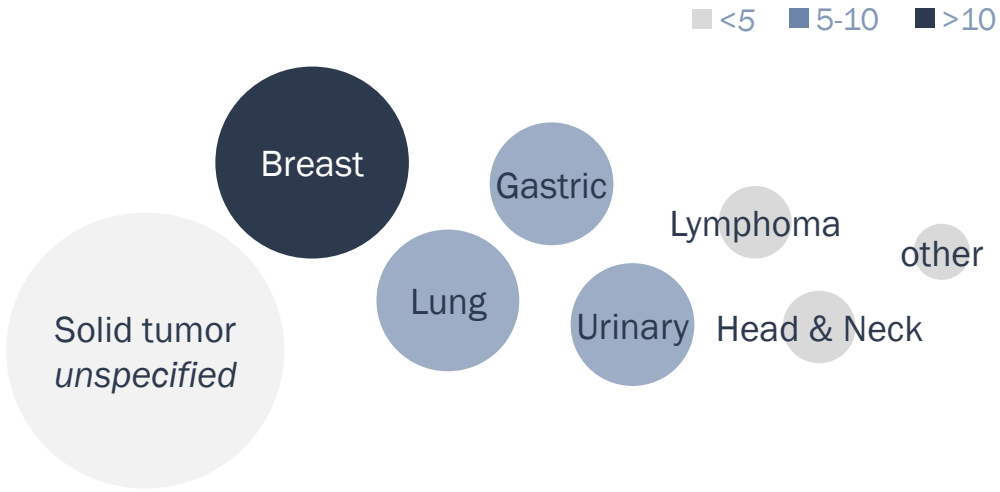
By originator geography:



Breast, lung, gastric and urinary cancers are the focus

Clinical stage ADCs developed by Chinese companies (N=55)

By indications (Chinese ADCs only):



- *HER2, Trop2, CLDN18.2 and Nectin-4 are the most frequently developed targets by Chinese ADC players*
- *Chinese ADC companies are also moving fast on next-generation technologies, such as bispecific ADCs*

U.S. ADCs still lead the field in terms of data maturity and first-in-class status; Chinese ADCs are catching up fast with technical improvements

Source: PharmaProjects; China ADC market deep-dive by Huajin Securities

Chinese companies are leaders in CAR-T therapies; a few of them are developing universal CAR-Ts

R&D

20+ Chinese companies are actively developing CAR-T therapies with 700+ clinical trials

Among them, many are exploring US market:

Company	Trials in	Drug	Highest Dev Phase*
CARSGEN THERAPEUTICS	US, Canada	CT041, (FDA RMAT & EMA Priority) CT071	Phase II
GenScript LEGEND BIOTECH	US	LB1908, LB2102	Phase I
BioSyngen	US	BRG01	*Phase II trial approved*
IASO BIOTHERAPEUTICS	US	CT103A (FDA ODD) CT120 (FDA ODD)	Phase Ib
易慕峰 IMMUNOFOCO	US	IMC 001 (FDA ODD) IMC 002 (FDA ODD)	Phase I
...			

Only a few are developing "off-the shelf" CAR-T:

GenScript LEGEND BIOTECH	Self-developed off-the-shelf CAR-T platform, with 4 products in Phase I, targeting CD19, CD 20 and BCMA
茂行生物 MAXIMUM BIOLOGY	MT-027, anti-B7H3 universal CAR-T, obtained FDA ODD and is applying for IND in the US for glioma
Innovent	"modular" Claudin 18.2-targeting CAR-T (IBI345), licensed out by Roche, currently in Phase I

Chinese CAR-T companies are running a large number of clinical trials, including for universal CAR-Ts

*Highest development phase only consider their development in overseas markets, excluding China
Note: RMAT – regenerative medicine advanced therapy; ODD – orphan drug designation

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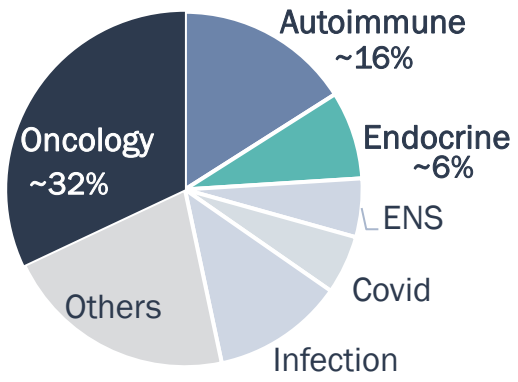
Besides oncology, autoimmune and endocrine diseases are major areas of innovation in China. Many GLP-1R, GIPR drugs are in development, including orally delivered molecules

R&D

Oncology is still a major focus for new therapies

2023 NMPA Approved Novel Therapy by Indication*



**Only NMPA approved new therapies in 2023, not including indication updates.*

Chinese companies have quickly entered the GLP-1 competition*

	Phase II	Phase III	NDA	Marketed
GLP-1R	甘李 GZR18	I-MAB BIOPHARMA TG103		仁会生物 BENEMAE Beinaglutide
	HENGRUI HRS-7535			
	闻泰医药 INCENTAGE VCT220	SCIWIND 先为达生物 Ecnoglutide		
GIPR/GLP-1R	翰森制药 HANSOH PHARMA HS-20094	HENGRUI Noiiglutide	HENGRUI HRS9531	
	众生药业 Zhongsheng Pharmacy RAY1225	BrightGene 博瑞医药 BGM0504		
Others	东阳光 HEC88473 (GLP-1/FGF21)			Innovent Mazdutide (GCGR/GLP-1R)

Chinese companies also follow global trend in choosing pipeline products and can move quickly into the "hot spots"

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Note: **Generics, bio-similar products are not included; NMPA – national medical product administration (of China)*

Key: Oral Tablet

By 2023, NMPA has streamlined accelerated approval programs which led to rapid approvals of many innovative drugs to address high medical needs

NMPA consolidated 5 accelerated approval programs

- Drugs addressing urgent clinical needs but not yet approved in China (*official list available*)
- Pediatric drugs/formulations/dosing with extra IND and NDA support (*official list available*)
- Innovative Vaccines in high demand
- Drugs approved as Breakthrough Therapy (*application process available each year*)
- Conditional approvals for drugs treating life-threatening diseases without existing treatments or to manage public health crisis
- Other priority drugs recognized by NMPA

Select drugs approved through priority channels in 2023

Drug	Priority Channel	Approval Time*	Indications
Aliqopa (copanlisib) 60 mg vial for injection	Conditional Approval	7 months	FL
COLUMVI glofitamab-gxbm injection for intravenous use 2.5 mg | 10 mg	Conditional Approval	9 months	DLBCL
Kadcyla ado-trastuzumab emtansine 20 mg/mL INJECTION FOR INTRAVENOUS USE	Breakthrough Therapy	10 months	BC
Kineret (anakinra)	Breakthrough Therapy	15 months	FMF
Koselugo (selumetinib) 10 mg & 25 mg capsules	Pediatric Drug Priority	12 months	Pediatric PN & NF1
Nexviazyme (avalglucosidase alfa-ngpt)	Orphan drug Priority	14 months	Pompe disease

China is speeding up the approvals for innovative drugs that meet high medical needs

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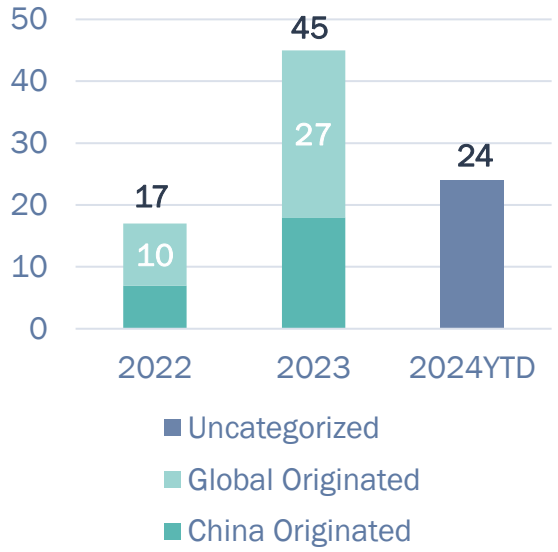
Note: *Approval time is defined as from the confirmation from NMPA for priority status until NMPA approval

China has dramatically accelerated the approval and accessibility of novel orphan drugs since 2023

China market access for orphan drugs continue to improve

NMPA approved orphan drugs



From 2019 to 2022, NMPA approved ~15 orphan drugs each year

Faster NMPA approvals

Orphan drugs can leverage priority channels for trial exemption and global trial inclusion to speed up approvals

Expanding orphan drug list

China has expanded the orphan disease list from 121 to 207 in 2023

Drug list of urgent clinical needs continues to be updated and includes more orphan drugs

New accessibility channels

Besides obtaining NMPA approvals, global orphan drugs are allowed to market in three special economic zones with regional registrations/approvals

China has been easing the regulatory approval and patient access to orphan drugs

NRDL has streamlined its inclusion policies making it possible for freshly approved products to enter NRDL within 12 months of approval

Payers

NRDL allows **novel therapy (or new indication) approved before June 30th to apply for NRDL the same year**

Price ceiling of NRDL listed products is set at 300K RMB (~$42K) per year per drug

The 2-year contract with NRDL can be **renewed without further price cut for exclusive products* without generics**

Each region adopts different **public medical reimbursement budget controls over high-priced drugs**

Products with NRDL contracts can be automatically moved to routine drug list when meeting three main criteria

Innovative products costing ≤300,000 RMB/ year can enter NRDL quickly to ramp up sales right after approval in China

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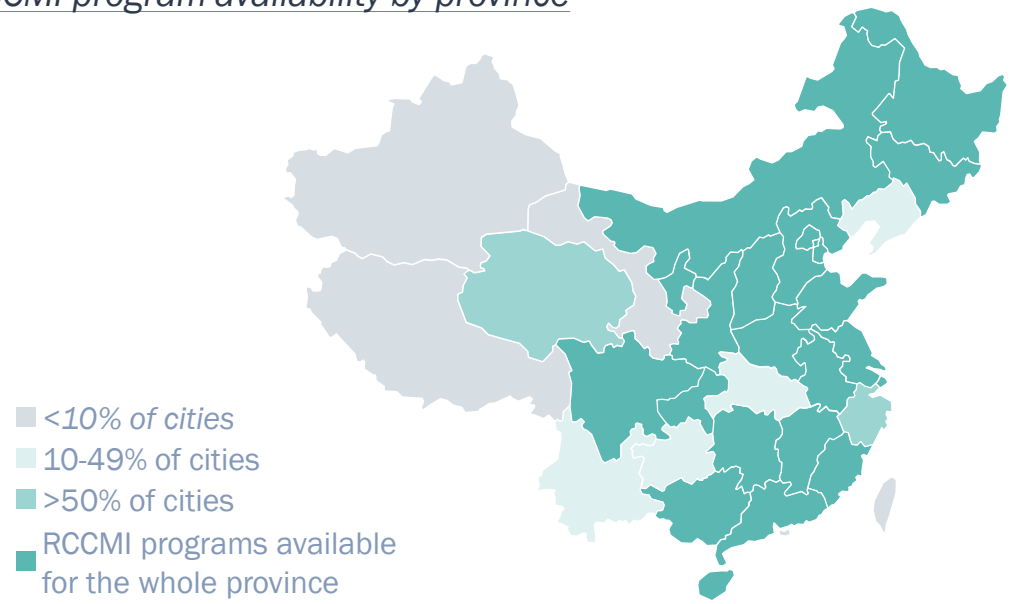
Note: *exclusive drugs – drugs within the patent period without marketed generics

Private paying system is in development, as RCCMI programs are spreading across China and have become very popular

Payers

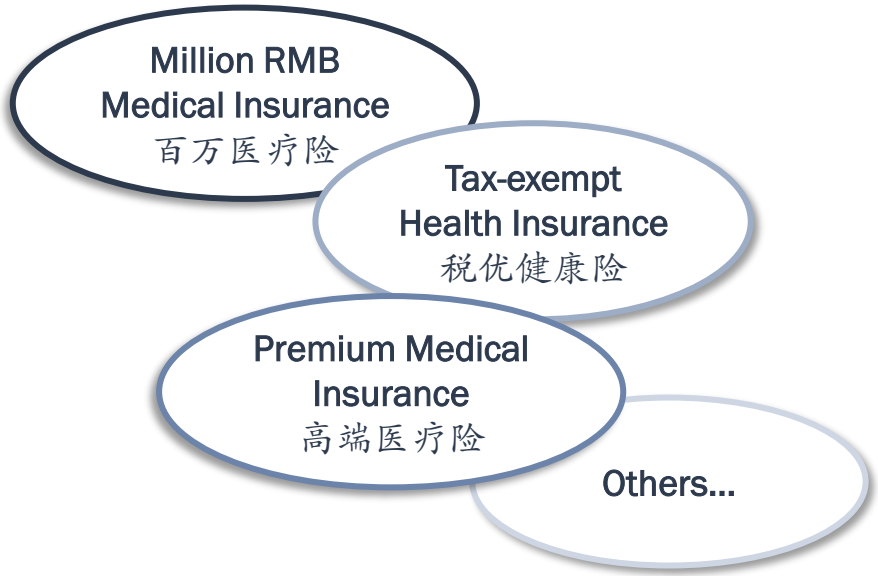
Regional Customized Commercial Medical Insurance (RCCMI) has been successfully rolled out across China since 2020

RCCMI program availability by province



~160 million enrollments in 2023

Facilitated by RCCMI, many other commercial programs are experiencing fast development



~300 million enrollments in 2023

Many novel therapies have achieved similar or better performances relying on private paying system which does not require significant price cut

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Sources : The connotation, current situation and sustainable development of regional customized commercial medical insurance by China LIFE; RCCMI program websites.

Severe price cuts from VBP led to product shortages, patient and physician distrust, which inadvertently boosted market position of high-end expensive products

Commercial

Case study: stenting

In 2020, the value-based procurement (VBP) of stenting devices **cut the prices by ~95%** and dropped the average VBP price **to $100-120/unit**

Companies **only** put their **low-end products through VBP** processes

Case study: insulin

In 2022, the value-based procurement of insulin products (2nd & 3rd-gen) **cut the prices by ~48%** and dropped the average VBP price **to $10-12/injection (3rd gen) and <$3-4/injection (2nd gen)**

Market reactions to VBP price cuts

- Mass shortage of VBP products and models
- Patients' association of poor quality with low costs
- Physicians' lack of incentive to use cheap products

- **High-end, non-VBP stent models ($2,500-11,500/unit)** are taking over the market
- **Drug-coated ballons (($2,000-3,000/unit)** are replacing cheap VBP stenting devices
- Since 2022, negative impacts on revenue and profitability have been minimized

- **3rd–gen insulin market share** increased from **58% to 70%** in 2 years
- **High-end non-VBP product, such as IDegLira (~$70/injection)** has reached $43 million revenue in 2023 in its first year on market
- Some global companies have **tripled their insulin revenue** since 2022

VBP price cuts drastically boosted market share of high-end products in China

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Note: PTCA - percutaneous transluminal coronary angioplasty; DCB – drug coated balloon

The booming growth of online medical consultation platforms and internet pharmacies have become a prominent sales channel for pharma products

Big pharma companies are investing in internet platforms as new marketing & sales channels

AstraZeneca

Invested in an internet company with 90K+ registered physicians offering consultation and O2O* drug deliveries

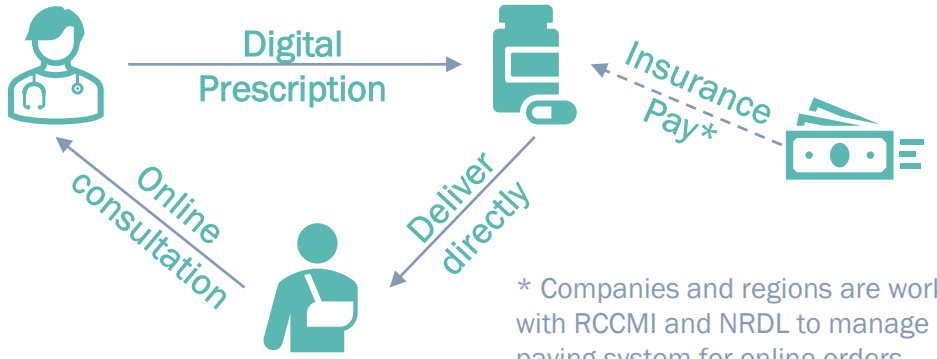
sanofi + JD.COM

Online platform targeting diabetes management, from drug refills to commercial insurance claims

Lilly + Tencent

Diabetes management app providing actual physician consultation, drug refill and other patient services

Digital prescription + DTP (direct-to-patient) pharmacy model is developing rapidly



* Companies and regions are working with RCCMI and NRDL to manage direct paying system for online orders

Online channel is rapidly growing in fields of:

- **Generic drugs** for common and simple diseases
- Drug refills for **chronic diseases**
- **High-cost novel therapies** (especially non-NRDL ones)

A consumer-oriented market for pharmaceuticals is forming
Pharma companies are developing online sales models for drug refills and patient management

*Note: O2O – online to offline

With the year-long healthcare anti-corruption campaign ending, market is rejuvenated with innovative therapies and patient services models

Boosting innovative therapies

CDE has sped up in reviewing and processing IND and NDA applications

Limits and executional controls on generic prices have led companies to put more efforts and investments in R&D

Encouraging self-sustainability

Biotech companies have refocused their attention to business development, as larger ones are investing in sales and marketing while smaller ones are searching for M&A opportunities rather than looking for investors

Focusing on product advantages

Drug sales and marketing are more regulated, leaving less incentives for prescribing poorer-performance drugs

Significant improvements on efficacy, safety and QoL are highly valued

Adapting policies to market

Policymakers modify policies and regulations to balance between social responsibilities and business development

New policies are quickly adjusted when severe market disruption emerges

Emphasizing patient service

Patient-facing auxiliary services have become an important sales lever, especially among competitors with products that offer similar perceived benefits

Chinese pharma market is heading towards a more regulated, product-based and market-driven environment, refocusing competition on product performance and patients

Acronyms

- **BC** – breast cancer
- **CDE** – center for drug evaluation, NMPA
- **CLL** – chronic lymphocytic leukemia
- **DLBCL** – diffuse large B-cell lymphoma
- **DTP** – direct to patient
- **ESCC** – esophageal squamous cell carcinoma
- **FL** – follicular lymphoma
- **FMF** – familial Mediterranean fever
- **MCL** – mantle cell lymphoma
- **mCRC** – metastatic colorectal cancer
- **MM** – multiple myeloma
- **MZL** – marginal zone lymphoma
- **NF1** – neurofibromatosis type 1
- **NMPA** – national medical products administration
- **NPC** – nasopharyngeal carcinoma
- **NRDL** – national reimbursement drug list
- **ODD** – orphan drug designation
- **PN** – plexiform neurofibromas
- **RCCMI** – regional customized commercial medical insurance
- **RMAT** – regenerative medicine advanced therapy
- **SLL** – small lymphocytic lymphoma
- **VBP** – value-based purchasing
- **WM** – Waldenstrom macroglobulinemia

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