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Initiation

Sector Report Healthcare

Picking certainty ahead of the great consolidation

24 October 2022

INVESTMENT SUMMARY

- We round out our coverage of Chinese innovative drug developers with three BUY's for BeiGene (BGNE), RemeGen and Akeso; three SELL's for Innovent, JUNSHI and Legend Bio (LEGN). We downgrade Zai Lab from BUY to HOLD;
- China's biotech industry started only in 2018 and now has 61 stocks, among which, only one (BGNE) is investible and two (RemeGen and Akeso) are on the way to become investable, in our view, at present time. Many Chinese biotech's will soon run out of cash and Chinese health regulators will tighten clinical standards in the next rounds of approvals. We also believe US-China rivalry will impact biotech;
- We, however, are cautiously optimistic on continuous development of China's biotech industry to eventually reach ~1/4 of the US over a course of two decades. More investible companies will emerge;
- Major headwinds are (1) shrinking value of the domestic market, (2) US-China rivalry. Major tailwinds are (1) acting as global deflation force for drug prices, (2) generic substitution at home and (3) policy support.

Research Team

Tianli Wen
Head of Research

Victor Yang
Head of Healthcare team

☎ +852 21856112
research@blue-lotus.cn

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A global deflation force but in its first inning

- Despite (1) persistent pricing pressure from China's state healthcare complex and (2) US-China rivalry likely spreading from semiconductor to biotech, we believe global deflation force and generic substitution are valuation supports;
- Three quarters of Chinese biotech industry may perish in the next two years yet it doesn't conflict with its eventually turning into the world's 2nd largest;
- We endorse BGNE for its global footprint and well-rounded competencies. We believe RemeGen is undervalued. We believe Akeso is becoming a biopharma.

Not all biotech's can, or should and will turn into biopharma's

As orchestrator of an inherently global industry, pharma/biopharma is desirable by many. But we believe the biotech-to-biopharma transformation is fraught with peril, more so now. After adopting loose approval policy for ~5 years, CDE/NMPA is showing signs of tightening up. NDRL price negotiation has permanently reset the market size expectation of Chinese innovative drugs. Yet many Chinese biotech's are still embarking on the journey to biopharma by building out sales and manufacturing. We believe a lot will end badly as their cashes run out.

Global price deflator role is valid, but validity is not assured

China's potential as a global drug price deflator is amply demonstrated in the development and pricing of PD-1/L1. More will come and come better. But the US innovative drug industry isn't without recourse. Controlling the pace of generic substitution is its build-in adjustment mechanism. Chinese innovation must happen fast enough to defeat this mechanism to justify the raison d'être.

A demand choke vs. a supply choke

A critical weakness exists in the argument of buying Chinese biotech, which is China's low cost of R&D must be low enough to offset its low drug price. Such modus operandi is inferior to the Western reverse model of selling drug at high price but outsourcing R&D to China or India. While biotech doesn't have a single supply chain choke point like the EUV lithography, it does have a demand choke point in which US alone is >40% of the world market. Chinese biotech/biopharma's must learn to deal with the US for a long time to come.

Key financials of stocks mentioned

	Revenues			Non-IFRS/GAAP Op. profit			IFRS/GAAP Net Income		
(mn)	2021	2022E	2023E	2021	2022E	2023E	2021	2022E	2023E
BeiGene (USD)	1,176	1,391	2,970	(1,198)	(1,537)	(235)	(1,398)	(1,977)	(829)
RemeGen (Rmb)	1,424	974	2,196	182	(935)	(434)	276	(797)	(355)
Akeso (Rmb)	226	567	1,682	(1,183)	(1,332)	(1,030)	(1,258)	(1,241)	(1,029)
ZAI LAB (USD)	144	207	291	(659)	(317)	(369)	(703)	(412)	(438)
Legend Bio (USD)	90	182	388	(353)	(405)	(782)	(296)	(390)	(821)
Innovent (Rmb)	4,270	4,626	5,665	(2,121)	(2,350)	(2,321)	(3,138)	(2,472)	(3,007)
JUNSHI (Rmb)	4,025	1,436	1,250	(492)	(2,931)	(3,261)	(728)	(2,994)	(3,396)

Source: BeiGene, RemeGen, Akeso, Zai Lab, Legend Bio, Innovent, JUNSHI, Blue Lotus (as of 2022/10/21)

Exhibit 1.

See the last page of the report for important disclosures

BUY **HOLD** SELL

Top picks

	Ticker	Rating	Target
BeiGene, Ltd.	BGNE US	BUY	US$197

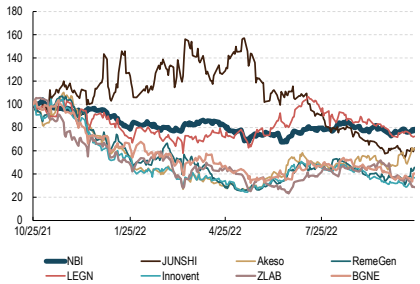
Source: Blue Lotus (as of 2022/10/21)

Stocks mentioned

Name	BBG code	Rating	TP	Curr. Price	Next yr PS
BeiGene	BGNE US	BUY	US$197	169.4	6.5
RemeGen	9995 HK	BUY	HK$70	46.65	10
Akeso	9926 HK	BUY	HK$40	31.00	17
Zai LAB	ZLAB US	HOLD	US$30	28.69	9.4
Legend Bio	LEGN US	SELL	US$16	47.63	19
Innovent	1801 HK	SELL	HK$17	30.20	8.0
JUNSHI	1877 HK	SELL	HK$6.0	25.20	17
HENGRUI	600276 CH	NR	NA	39.97	9.6
SinoBio	1177 HK	NR	NA	4.2	2.1
CARsgen	2171 HK	NR	NA	13.58	123
FOSUN Ph.	2196 HK	NR	NA	19.60	1.5

Source: Blue Lotus (coverage), Bloomberg (as of 2022/10/21)

Price performance and volume data



Source: Bloomberg, Blue Lotus (as of 2022/10/21)

Research team

Tianli Wen
Head of Research

Weiqing Yang
Head of Pharma & Biotech

☎ +852 21856112
research@blue-lotus.cn

Financial Summary - BeiGene, LTD

Fiscal year ends-31-Dec

Exhibit 2. Income statement

(US$ mn)	2021A	2022E	2023E
Revenue	1,176	1,391	2,970
Cost of sales	(165)	(286)	(394)
Gross profit	1,011	1,105	2,576
Gross margin	86.0%	79.4%	86.7%
Operating expense	(2,450)	(2,938)	(3,406)
Research and development costs	(1,459)	(1,629)	(1,792)
Selling, general and administrative	(990)	(1,308)	(1,611)
Amortization of intangible assets	(1)	(1)	(3)
Share based compensation	(241)	(295)	(594)
Operating income (GAAP)	(1,439)	(1,833)	(829)
Operating margin, GAAP	(122%)	(132%)	(28%)
Operating income (non-GAAP)	(1,198)	(1,537)	(235)
Operating margin, non-GAAP	(102%)	(111%)	(8%)
Loss/Profit before income tax	(1,423)	(1,951)	(829)
Profit/loss for the year from continuing operations	(1,398)	(1,977)	(829)
Basic shares	93	105	109
Diluted shares	103	115	119
EPADS, basic and diluted	(15.06)	(18.87)	(7.62)

Source: BeiGene, LTD., Blue Lotus (2022/10/21)

Company Description

BeiGene (BGNE) is one of China's oldest biotech's and is now turning itself to be a product selling biopharma. Still, it remains R&D focused and generated 46% of its 2021 revenue of US$1.2bn from license-out. In-house developed BTK Inhibitor Zanubrutinib (*BRUKINSA*) and PD-1 Tislelizumab contributed 40% of revenues in 2021. License-in revenues from selling three Amgen drugs and two BMS drugs contributed 13% of revenues in 2021.

Industry View

We estimate the global biologics market to grow from US$341bn in 2021 to US$665bn in 2030, in which China's biologics market will grow from US$65bn to US$200bn over the same period.

Exhibit 3. Balance sheet

(US$ mn)	2021A	2022E	2023E
Current assets	7,614	5,340	5,076
Cash and cash equivalents	4,376	2,695	2,046
Short-term investments	2,242	1,381	1,048
Accounts receivable	483	487	891
Inventories	243	343	433
Prepaid expenses	270	434	658
Non-current assets	1,032	1,459	2,379
Property, plant and equipment	588	795	1,290
Right-of-use assets	117	229	348
Intangible assets	47	36	26
Deferred tax assets	110	139	297
Other non-current assets	163	252	412
Total assets	8,646	6,799	7,456
Current liabilities	1,600	1,619	2,309
Accounts payable	262	371	468
Accrued expenses	558	890	1,237
Deferred revenue	187	209	445
R&D cost share liability	121	78	35
Short-term debt	428	-	-
Non-current liabilities	803	536	723
Long-term debt	202	-	-
Deferred income	220	209	445
R&D cost share liability	270	182	82
Additional paid-in capital	11,191	11,567	12,174
Accumulated comp. income (loss)	18	20	22
Accumulated deficit	(4,966)	(6,944)	(7,773)
Equity	6,243	4,643	4,423
TOTAL LIABILITIES & EQUITY	8,646	6,798	7,455

Source: BeiGene, LTD., Blue Lotus (2022/10/21)

Exhibit 4. Cash flow state

(US$ mn)	2021A	2022E	2023E
Net loss (income), GAAP	(1,398)	(1,951)	(829)
Adjustment			
Depreciation and amortization expense	46	82	109
Share-based payment expenses	241	295	594
Acquired in-process R&D	84	90	95
Amortization of R&D cost share liability	(112)	(130)	(143)
Deferred income tax benefits	(44)	(29)	(158)
Operating cash flows	(1,168)	(1,643)	(332)
Increase in inventories	(153)	(101)	(90)
Increase in account receivables	(423)	(4)	(404)
Increase in prepaid expenses	(110)	(163)	(224)
Increase in account payables	30	109	97
Increase in accrued expenses	212	331	348
Increase in deferred income	408	10	474
Net cash used in operating activities	(1,185)	(1,412)	(61)
Capex	(263)	(278)	(594)
Purchase and ST investments	999	0	0
Purchase of in-process R&D	(84)	(90)	(95)
Payments for intangible assets	(43)	0	0
Other investing activities	0	0	0
Net cash used in investing activities	566	(368)	(689)
Proceeds and repayment LT loans	17	0	0
Proceeds and repayment ST loas	84	0	0
Others	3,535	100	100
Net cash used in financing activities	3,636	100	100
Cash at the beginning of the year/period	1,390	4,376	2,695
Cash at the end of the year/period	4,376	2,695	2,046

Source: BeiGene, LTD. Blue Lotus (2022/10/21)

See the last page of the report for important disclosures

Financial Summary - RemeGen Co., Ltd.:

Fiscal year ends-31-Dec

Exhibit 5. Income statement

(RMB mn or Rmb)	2021A	2022E	2023E
Revenues	1,424	974	2,196
Cost of sales	(67)	(359)	(445)
Gross profit	1,357	615	1,751
operating expense	(1,194)	(1,580)	(2,251)
Selling and distribution expenses	(263)	(320)	(432)
Administrative expenses	(220)	(279)	(517)
Research and development expenses	(711)	(981)	(1,301)
Operating income (IFRS)	163	(965)	(500)
Other income and gains	186	206	196
Other expenses	(67)	(27)	(45)
Impairment losses on financial assets, net	(0)	(7)	(2)
Finance costs	(5)	(4)	(4)
Loss/Profit before income tax	276	(797)	(355)
Income tax expense	-	-	-
Profit/Loss for the year, IFRS	276	(797)	(355)
Loss/profit attr to SH	276	(797)	(355)
Loss per share, IFRS	0.68	(1.86)	(0.81)

Source: RemeGen Co., Ltd., Blue Lotus (2022/10/21)

Company Description

RemeGen was founded in 2008 in Yantai, Shandong Province of China. It focuses on Antibody Drug Conjugate (ADC), Bispecific Antibody (BsAb) and Fusion Protein drugs in Autoimmune, Oncology and Ophthalmology. Its first drug Telitacicept (RC18), a fusion protein for Systemic Lupus Erythematosus (SLE) was approved in China in March 2021 and contributed 3.3% of revenues in 2021. Its 2nd drug, Disitamab Vedotin (RC48), an ADC for solid tumors, was approved in July 2021 in China and contributed 6.1%. License-out revenue contributed 91%.

Industry View

We estimate China's total biologics market to grow to US$68 bn in 2021, and will grow to US$200 bn by the end of 2030. We expect that the global total biologics market to grow to US$345 bn in 2021, and will reach US$768 mn in 2030. We expect the global ADC market to grow from US$5.8nm in 2021 to US$23bn in 2030.

Exhibit 6. Balance sheet

(RMB mn or Rmb)	2021A	2022E	2023E
Property, plant and equipment	1,578	2,037	2,659
Right-of-use assets	149	139	186
Other intangible assets	13	20	38
Equity investments	12	-	-
Other non-current assets	108	116	152
Inventories	280	1,077	891
Trade and bills receivables	7	75	179
Prepayments,	177	566	299
Pledged deposits	79	-	-
Cash and cash equivalents	1,757	4,968	4,245
Total assets	4,159	8,998	8,649
Trade and bills payables	159	538	445
Other payables and accruals	393	1,795	1,781
Lease liabilities	52	24	48
Deferred income	4	12	23
Other current liabilities	7	34	38
Lease liabilities	50	40	81
Deferred tax liabilities	0	20	-
Deferred income	46	20	40
Total liabilities	713	2,482	2,457
Share capital	490	490	490
Treasury shares	(449)	3,471	3,486
Paid-in capital	-	-	-
Reserves	3,406	2,609	2,254
Total equities and liabilities	4,159	8,998	8,649

Source: RemeGen Co., Ltd., Blue Lotus (2022/10/21)

Exhibit 7. Cash flow state

(RMB mn or Rmb)	2021A	2022E	2023E
Pre-tax profit	276	(797)	(355)
Adjustment			
Finance costs	5	4	4
Deprecaition & Amortization	118	196	258
Share-based payment expenses	19	30	66
Increase in inventories	(214)	(796)	186
Decrease in bills receivable	(7)	(68)	(104)
Increase in prepayments,	(75)	(388)	266
Increase/(decrease) in trade payables	97	379	(93)
Increase in other payables and accruals	182	1,401	(13)
(Increase)/decrease in pledged deposits	38	(79)	-
Others	106	(95)	10
Net cash used in operating activities	547	(213)	225
Purchases of items of PPE	(850)	(603)	(837)
Increase in pledged deposits	(38)	79	-
Others	(56)	(52)	(111)
Net cash used in investing activities	(944)	(576)	(948)
New bank borrowings	(108)	-	-
Proceeds from issue of common shares	-	4,000	-
Others	(55)	-	-
Net cash used in financing activities	(163)	4,000	-
Net change in cash	(561)	3,211	(723)
Effects of foreign exchange rate changes	(10)	-	-
Cash and equivalent at beginning	2,769	1,757	4,968
Cash and equivalent at end	1,757	4,968	4,245

Source: RemeGen Co., Ltd., Blue Lotus (2022/10/21)

See the last page of the report for important disclosures

Financial Summary - Akeso Inc.

Fiscal year ends-31-Dec

Exhibit 8. Income statement

(RMB mn or Rmb)	2021A	2022E	2023E
Product sales	212	869	2,076
License fee income	129	0	0
Less: distribution cost	(115)	(301)	(394)
Revenue	226	567	1,682
Gross profit	194	473	1,331
Gross margin	86.1%	83.3%	1
Selling and marketing expenses	(179)	(362)	(788)
Administrative expenses	(244)	(254)	(310)
Research and development expenses	(1,123)	(1,242)	(1,431)
Other expenses	(13)	(110)	(252)
Share based compensation	(181)	(54)	(168)
Operating income (IFRS)	(1,248)	(1,210)	(999)
Operating margin, IFRS	(553%)	(213%)	(59%)
Operating income (non-IFRS)	(1,183)	(1,332)	(1,030)
Operating margin, non-IFRS	(524%)	(235%)	(61%)
Net income, IFRS	(1,258)	(1,241)	(1,029)
EPS, diluted and basic	(1.54)	(1.52)	(1.26)

Source: Akeso Inc., Blue Lotus (2022/10/21)

Company Description

Akeso is about to transform from an IP-licensing biotech to a product-sales-driven biopharma. Its products and pipeline focus on BsAb and mAb with 100% in-house ratio. Penpulimab (AK105), co-marketed with SinoBio, contributed 100% of product revenue and 62% of total in 2021. Cadonilimab (AK104) shall drive product revenue to 100% of total in 2022. Through its in-house ACE Platform and TETRABODY technology, Akeso has established a systematic process for drug development.

Industry View

We estimate the global biologics market to grow from US$341bn in 2021 to US$665bn in 2030, in which China's biologics market will grow from US$65bn to US$200bn over the same period. We expect global PD-1/L1 market to grow from US$30bn in 2021 to US$79bn in 2030, in which China's PD-1/L1 market to grow from US$4bn to US$20bn.

Exhibit 9. Balance sheet

(RMB mn or Rmb)	2021A	2022E	2023E
Non-current assets	1,654	2,740	3,940
PPE	1,353	2,105	2,438
Right of use assets	152	623	1,488
Intangible assets	4	2	4
Advance payments for PPE	145	10	10
Current assets	3,152	2,191	7,601
Inventories	197	520	2,277
Trade and bill receivables	102	418	1,557
Prepayments and other receivables	212	784	1,245
Bank balances and cash	2,642	469	2,521
Total assets	4,806	4,931	11,541
Current liabilities	656	1,462	3,582
Trade payables	206	577	1,401
Other payables and accrued exp.	395	852	2,102
Interest bearing borrowings	46	-	-
Lease liabilities	8	32	77
Non-current liabilities	870	813	1,826
Interest bearing borrowings	804	804	1,804
Deferred income	64	245	306
Total liabilities	1,526	2,275	5,408
Reserves	3,164	1,923	895
Non-controlling interest	116	733	5,239
Equities	3,280	2,656	6,134
Total liabilities and equities	4,806	4,931	11,541

Source: Akeso Inc., Blue Lotus (2022/10/21)

Exhibit 10. Cash flow state

(RMB mn or Rmb)	2021A	2022E	2023E
Pre-tax profit, IFRS	(1,258)	(1,241)	(1,029)
Adjustment from operating activities	142	99	259
Adjustment from balance sheet			
Increase in inventories	(135)	(324)	(1,757)
Increase in trade-receivables	(102)	(316)	(1,139)
Increase in prepayments	(68)	(572)	(462)
Increase in trade payables	94	371	824
Increase in other payables	355	457	1,251
Increase in deferred income	10	181	61
Increase in contract liabilities	4	31	58
Cash used in/generated from operations	(958)	(1,314)	(1,933)
Income tax paid	0	0	0
Net cash used in operating activities	(958)	(1,314)	(1,933)
Interest received	14	11	10
Capex	(793)	(869)	(519)
Purchase of intangible assets	(4)	(2)	(6)
Proceeds from disposal of PPE	1	1	1
Decrease in pledged deposits	1,853	0	0
Net cash used in investing activities	1,071	(859)	(514)
New borrowings raised less repayment	672	0	1,000
Net cash used in financing activities	1,633	0	4,500
Cash and cash equivalents at the beginning	2,684	2,642	469
Effects of foreign exchange rate changes	0	0	0
Cash and cash equivalents at the end	2,642	469	2,521

Source: Akeso Inc., Blue Lotus (2022/10/21)

See the last page of the report for important disclosures

Financial Summary – Legend Biotech

Fiscal year ends 31-Dec

Exhibit 11. Income statement

(US$ mn)	2021A	2022E	2023E
Revenues	90	182	388
Cost of sales	90	147	302
Gross profit	90	147	302
Gross margin over net revenues	100%	81%	78%
Operating expense	(463)	(571)	(1,123)
Research and development expenses	(313)	(366)	(776)
Administrative expenses	(47)	(91)	(152)
Selling, general and administrative	(103)	(114)	(195)
Share based compensation	(20)	(19)	(39)
Operating income, GAAP	(373)	(424)	(821)
Operating margin, GAAP	(415.4%)	(233.4%)	(211.7%)
Operating income, non-GAAP	(353)	(405)	(782)
Operating margin, non-GAAP	(393.0%)	(222.9%)	(201.7%)
Loss/Profit before income tax	(386)	(390)	(821)
Pre-tax margin	(429.4%)	(215.0%)	(211.7%)
Net loss/income, GAAP	(296)	(390)	(821)
Net margin, GAAP	(329.4%)	(215.0%)	(211.7%)
EPADS, on diluted and basic, GAAP	(2.10)	(2.27)	(4.18)

Source: Legend Biotech,, Blue Lotus (2022/10/21)

Company Description

Legend Biotech is a global, clinical-stage cell therapy company dedicated to treating, and one day curing, life-threatening diseases. Its pipelines include autologous and allogenic chimeric antigen receptor T-cell, T-cell receptor (TCR-T), and natural killer (NK) cell-based immunotherapy. Also, it collaborates with leading global biopharma companies to advance its product commercialization.

Industry View

We estimate China's total biologics market to grow to US$106 bn in 2024, and will grow to US$200 bn by the end of 2030. We expect that the global total biologics market to grow to US$457 bn in 2024, and will reach US$768mn in 2030.

Exhibit 12. Balance sheet

(US$ mn)	2021A	2022E	2023E
Non-current assets	170	395	574
Property, plant and equipment, net	146	213	343
Time deposits	5	155	155
Intangible assets, net	5	9	18
Current assets	949	661	1,365
Inventories	2	17	43
Trade receivables	50	121	288
Prepayments and other current assets	13	26	43
Financial assets measured at cost	30	0	0
Time deposits	164	14	14
Cash and cash equivalents	689	483	977
Total assets	1,118	1,056	1,939
Current liabilities	280	229	439
Account payables	7	5	17
Other payables and accruals	123	174	389
Contract liabilities	61	48	28
Non-current liabilities	367	515	637
Interest-bearing loans and borrowings	120	320	520
Contract liabilities	243	192	110
Total liabilities	647	744	1,076
Equity	471	312	862
Total liabilities and equity	1,118	1,056	1,939

Source: Legend Biotech,, Blue Lotus (2022/10/21)

Exhibit 13. Cash flow statement

(US$ mn)	2021A	2022E	2023E
Loss before tax	(386)	(390)	(821)
Adjustments			
Finance income	(1)	(3)	(4)
Finance costs	1	4	4
Depreciation of property and equipment	11	17	25
Amortization of intangibles	1	2	4
Share-based compensation	20	19	39
Changes in operating assets and liabilities:	21	(117)	(85)
Accounts receivable	25	(71)	(167)
Prepayments and other current assets	(3)	(13)	(17)
Inventories	0	(15)	(25)
Accounts payable	2	(2)	12
Other payables	24	51	214
Contract liabilities	(27)	(64)	(102)
Net cash used in operating activities	(332)	(467)	(837)
Cashflows from investing activities:	(44)	(82)	(155)
Purchase of property and equipment	(3)	(6)	(14)
Purchase of intangible assets	(3)	(6)	(14)
Net cash used in investing activities	(166)	62	(169)
Proceeds from follow on offering	323	0	0
Proceed from private placement	300	0	1,500
Proceeds from borrowing and repayment	0	200	200
Net cash provided by financing activities	623	200	1,500
Cash, cash equivalents - beginning of the year	456	689	483
Cash, cash equivalents — end of the year	689	483	977

Source: Legend Biotech., Blue Lotus (2022/10/21)

Financial Summary - Innovent Biologics, Inc.

Fiscal year ends-31-Dec

Exhibit 14. Income statement

(RMB mn or Rmb)	2021A	2022E	2023E
Revenue	4,270	4,626	5,665
Cost of sales	(573)	(1,037)	(1,564)
Gross profit	3,697	3,589	4,101
Gross margin	86.6%	77.6%	72.4%
Other income	197	205	300
Operating expense	(6,809)	(6,558)	(7,272)
Administrative expenses	(884)	(885)	(928)
Selling and marketing expenses	(2,728)	(2,710)	(2,960)
Royalty and other related payments	(719)	(535)	(708)
Share based compensation	(904)	(619)	(850)
Operating income (IFRS)	(2,989)	(2,374)	(2,871)
Operating margin	(70.0%)	(51.3%)	(50.7%)
Operating income (non-IFRS)	(2,121)	(2,350)	(2,321)
Operating margin	(49.7%)	(50.8%)	(41.0%)
Loss/Profit before income tax	(3,051)	(2,472)	(3,007)
Pre-tax margin	(71.5%)	(53.4%)	(53.1%)
Profit/loss for the year from continuing operations	(3,138)	(2,472)	(3,007)
EPS, diluted and basic	(2.16)	(1.68)	(2.03)

Source: Innovent Biologics, Inc., Blue Lotus (2022/10/21)

Company Description

Innovent Biologics is a Chinese biopharma with ambitious plan to build out an R&D and commercialization platform. In 2021, product sales constituted 94% of Innovent's total revenue of Rmb4.3bn, among which Sintilimab contributed 2/3 of product sales while biosimilars contributed the remaining 1/3. We expect license-in to contribute ~10% of product sales in 2022.

Industry View

We estimate the global biologics market to grow from US$341bn in 2021 to US$665bn in 2030, in which China's biologics market will grow from US$65bn to US$200bn over the same period.

Exhibit 15. Balance sheet

(RMB mn or Rmb)	2021A	2022E	2023E
Non-current assets	4,693	5,538	5,941
PPE	2,693	3,592	3,809
Right of use assets	397	539	571
Intangible assets	772	937	1,103
Equity instruments at FVOTCI	203	203	203
Deposits for acquisition of PPE	286	10	10
Other receivables	128	133	133
Other financial assets	645	612	555
Current assets	11,551	10,205	10,647
Inventories	1,347	2,194	2,978
Trade receivables	968	1,049	1,285
Prepayments and other receivables	213	231	283
Other financial assets	645	612	555
Bank balances and cash	8,377	6,118	5,547
Total assets	16,244	15,743	16,588
Current liabilities	3,050	4,578	6,214
Trade payables	195	353	532
Other payables and accrued exp.	2,052	3,342	4,535
Contract liabilities	356	519	782
Borrowings	365	365	365
Non-current liabilities	2,863	2,712	4,038
Contract liabilities	356	519	782
Borrowings	365	365	365
Government grants	295	170	233
Total liabilities	5,913	7,290	10,251
Equity	10,330	8,452	6,337
Reserves	10,330	8,452	6,337
TOTAL LIABILITIES AND EQUITY	16,244	15,743	16,588

Source: Innovent Biologics, Inc., Blue Lotus (2022/10/21)

Exhibit 16. Cash flow state

(RMB mn or Rmb)	2021A	2022E	2023E
Pre-tax profit, IFRS	(3,051)	(2,472)	(3,007)
Adjustment			
Depreciation of PPE	165	257	349
Amortization	3	77	102
Depreciation of right of assets	37	57	78
Share based compensation	904	619	850
Bank interest income	(152)	(145)	(117)
Interest on bank borrowings	77	107	130
Operating cash flows	(2,013)	(1,498)	(1,614)
Increase in inventories	(642)	(847)	(783)
Increase in trade receivables	(493)	(81)	(236)
Increase/(decrease) in prepayments	(49)	(18)	(52)
Increase in trade payables	74	158	179
Increase in other payables	1,078	1,290	1,193
Increase in contract liabilities	105	223	527
Increase in government related income	249	(124)	62
Cash used in/generated from operations	(1,689)	(897)	(724)
Net cash used in operating activities	(1,776)	(897)	(724)
Capex	(1,275)	(1,156)	(566)
Purchase of intangible assets	(742)	(243)	(268)
Net cash used in investing activities	(1,866)	(1,254)	(718)
Interest paid	(77)	(107)	(130)
New borrowings raised and repayment made	1,208	0	1,000
Issuance of ordinary shares	3,940	0	0
Net cash used in financing activities	5,005	(107)	870
Net increase in cash	1,363	(2,259)	(572)
Cash and equivalents at beginning	7,764	8,377	6,118
Cash and equivalents at end	8,377	6,118	5,547

Source: Innovent Biologics, Inc., Blue Lotus (2022/10/21)

See the last page of the report for important disclosures

Financial Summary - Shanghai Junshi Biosciences Co. Ltd.

Fiscal year ends-31-Dec

Exhibit 17. Income statement

(RMB mn or Rmb)	2021A	2022E	2023E
Revenue	4,025	1,436	1,250
Cost of sales	(1,258)	(579)	(723)
Gross profit	2,767	857	527
Total operating expense	(3,451)	(3,865)	(3,850)
Research and development expenses	(2,069)	(2,562)	(2,750)
Selling and distribution expenses	(735)	(607)	(550)
Administrative expenses	(648)	(695)	(550)
Share based payments	(193)	(77)	(63)
Operating income, IFRS	(685)	(3,008)	(3,323)
Operating income (non-IFRS)	(492)	(2,931)	(3,261)
Loss/Profit before income tax	(593)	(2,984)	(3,396)
Profit/Loss for the year, IFRS	(728)	(2,994)	(3,396)
EPS, basic shares	(0.81)	(3.29)	(3.61)

Source: Shanghai Junshi Biosciences Co. Ltd., Blue Lotus (2022/10/21)

Company Description

JUNSHI is making an attempt to transition from a biotech to a biopharma. Its top selling PD-1/L1 drug Toripalimab (*TUOYI*) contributed 96% of its product sales of Rmb427mn. 2021 was a big year for JUNSHI's license-out revenues, up 8.2x to Rmb3.3bn but is unlikely to repeat in the future years.

Industry View

We estimate the global biologics market to grow from US$341bn in 2021 to US$665bn in 2030, in which China's biologics market will grow from US$65bn to US$200bn over the same period.

Exhibit 18. Balance sheet

(RMB mn or Rmb)	2021A	2022E	2023E
Non-current assets	5,219	3,867	3,708
Property, plant and equipment	2,728	2,768	2,725
Right-of-use assets	342	363	371
Intangible assets	40	40	50
Interests in associates	442	158	137
Prepayments and other rec's	534	138	75
Other financial assets	1,027	366	319
Current assets	5,832	3,316	3,234
Inventories	485	232	362
Trade receivables	1,293	1,370	1,900
Prepayments and other rec's	549	172	125
Bank balances and cash	3,505	1,542	848
Total assets	11,051	7,182	6,942
Trade and other payables	1,908	753	795
Contract liabilities	0	290	362
Current liabilities	2,017	771	817
Borrowings	490	1,490	4,490
Deferred income	119	42	37
Non-current liabilities	702	1,550	4,549
Total liabilities	2,719	2,320	5,366
Share capital	911	911	911
Reserves	7,050	4,056	660
Equity attributable to owners	7,961	4,967	1,571
Non-controlling interests	371	(105)	6
TOTAL LIABILITIES AND EQUITY	11,051	7,183	6,943

Source: Shanghai Junshi Biosciences Co. Ltd., Blue Lotus (2022/10/21)

Exhibit 19. Cash flow state

(RMB mn or Rmb)	2021A	2022E	2023E
Pre-tax profit, IFRS	(593)	(2,984)	(3,396)
Adjustment			
Bank interest income	(31)	(42)	(10)
Finance costs	22	27	80
Net gains from FV of financial assets	(114)	23	0
Depreciation of property, plant and equipment	225	319	355
Depreciation of right-of-use assets	45	51	54
Amortisation of intangible assets	5	7	8
Share-based payment expenses	193	77	63
Operating cash flows before movements in working capital	(145)	(2,582)	(2,848)
Increase in inventories	(141)	253	(130)
Decrease in trade receivables	(630)	(77)	(530)
Increase in prepayments	(478)	773	110
Increase in trade and other payables	693	(1,154)	42
(Decrease) increase in deferred income	64	255	79
Income tax paid	(138)	(9)	0
Net cash used in operating activities	(776)	(2,542)	(3,277)
Interest received	31	42	10
Payments for property, plant and equipment	(608)	(359)	(313)
Payments for intangible assets	(14)	(7)	(19)
Upfront payments for right-of-use assets	(201)	(72)	(63)
Others	(1,022)	45	47
Net cash used in investing activities	(1,814)	(393)	(337)
New borrowing and payment	(293)	1,000	3,000
Interest paid	(16)	(27)	(80)
Others	2,982	0	0
Net cash used in financing activities	2,672	973	2,920
Cash and cash equivalents at the beginning	3,385	3,505	1,542
Cash and cash equivalents at the end	3,505	1,542	848

Source: Shanghai Junshi Biosciences Co. Ltd., Blue Lotus (2022/10/21)

Financial Summary - Zai LAB Limited

Fiscal year ends-31-Dec

Exhibit 20. Income statement

(US$ mn or US$)	2021A	2022E	2023E
Revenues	144	207	291
Cost of sales	(52)	(71)	(99)
Gross profit	92	136	192
Operating expense	(792)	(508)	(634)
Selling and distribution expenses	(219)	(248)	(307)
Research and development expenses	(573)	(260)	(327)
Operating income (non-GAAP)	(700)	(372)	(442)
Other income (expense), net	(3)	(40)	4
Loss/Profit before income tax	(703)	(412)	(438)
Income tax expense	-	-	-
Profit/Loss for the year, GAAP	(703)	(412)	(438)
Loss/profit attr to SH	(703)	(412)	(438)
EPS, GAAP, basic and diluted	(7.58)	(3.86)	(3.95)

Source: Zai LAB, Blue Lotus (2022/10/21)

Company Description

Zai Lab (ZLAB) is a Chinese innovative drug distribution platform with a license-in model from biotech's globally. In 2021, 65% of its revenue came from product sales of *ZEJULA* (Niraparib), which ZLAB licensed, to sell in China. All ZLAB's late-stage pipeline drugs are licensed.

Industry View

We estimate the global biologics market to grow from US$341bn in 2021 to US$665bn in 2030, in which China's biologics market will grow from US$65bn to US$200bn over the same period.

Exhibit 21. Balance sheet

(US$ mn or US$)	2021A	2022E	Next year
Cash and cash equivalents	964	749	541
Short-term investments	445	245	45
Accounts receivable	47	68	94
Note receivable	7	0	0
Inventories	19	36	50
Other current assets	18	24	33
Property and equipment, net	43	65	95
Operating lease right-of-use assets	14	9	10
Land use rights, net	8	8	7
Intangible assets, net	2	2	3
Value added tax recoverable	24	30	37
Other non-current assets	18	18	19
Total assets	1610	1252	934
Accounts payable	126	107	124
Current operating lease liabilities	6	3	4
Other current liabilities	61	76	95
Non-current liabilities	37	41	50
Additional paid-in capital	2,826	2,850	2,917
Accumulated deficit	(1,418)	(1,830)	(2,268)
Accumulated other comprehensive income (loss)	(24)	5	12
Other equity	(4)	-	-
Total liabilities and shareholders' equity	1,610	1,253	934

Source: Zai LAB, Blue Lotus (2022/10/21)

Exhibit 22. Cash flow state

(US$ mn or US$)	2021A	2022E	2023E
Net loss	(704)	(412)	(438)
Depreciation and amortization	6	10	14
Share-based compensation	41	55	73
Accounts receivable	(42)	(20)	(27)
Inventories	(7)	(17)	(14)
Value added tax recoverable	(2)	(6)	(6)
Prepayments and other current assets	(7)	(6)	(9)
Accounts payable	64	(19)	17
Other current liabilities	19	15	19
Net cash provided by operating activities	(549)	(385)	(362)
Purchases and redemption of short-term investments	299	200	200
Purchase of property and equipment	(18)	(31)	(44)
Purchase of intangible assets	(1)	(1)	(1)
Net cash provided by investing activities	250	168	155
Proceeds from issuance of ordinary shares upon public offerings	819	-	-
Payment of public offering costs	(2)	-	-
Net cash provided by financing activities	820	-	-
Effect of exchange rate	1	-	-
Net decrease (increase) in cash and cash equivalents	521	(217)	(207)
Cash and cash equivalents at beginning of the year	443	966	749
Cash and cash equivalents at end of the year	965	749	541

Source: Zai LAB, Blue Lotus (2022/10/21)

Contents

Summary of our thoughts

- **The rise of Chinese biotech industry has a global calling**: PD-1/L1 drug prices in China, after domestic competition and NDRL price cuts, reached ~5% of those in the US. Certainly, these drugs came four years after FDA's first PD-1/L1 approval and thus the line with generic drug is blurred. But we are seeing and we can foresee the gap to be narrowing in new drug classes like CAR-T, BsAb/mAb, ADC and etc. The retirees at US may have big enough pension fund to pay for expensive drugs, but the world population can benefit from cheaper innovative drugs;

- **Chinse biotech's are still at the first inning of a two-decade run up**: There are currently 61 biotech stocks traded on HKSE, STAR SSE and Nasdaq, all of which went public after 2018. There are ~800 biotech stocks in US, of which ~200 has liquidity. Genentech, the first US biotech IPO, took place in 1980;

The fundamental of biotech is to achieve sustained revenue at high profit margins. The deal is to make this possible through regulatory protection.

- **Prematurely embarking on a transformation into biopharma will end badly**: Biotech sells IP while biopharma sells product. To do so the company must build sales force and manufacturing facilities. The alternative will be to license the drug sales out to pharma/biopharma and/or manufacturing out to CRO/CDMO's. Few Chinese biotech's have more than one in-house selling drugs. A handful has two and none has three. To fill the pipeline the company may opt for license-in and/or developing biosimilars. We believe such strategy, adopted by Innovent and JUNSHI, will diverge the company's focus and require demanding execution from the management. The outcome may not be positive, in our view, despite short term results;

- **Pricing and profit margin are keys to profitability**: The essence of innovative drug industry is to spend huge amount of R&D to embark on an uncertain journey of discovery. Yet the reward for first-in-class (FIC) discovery is prolonged intellectual property protection on pricing and gross margins. We argue that regardless of biotech, biopharma or pharma, such process remains the holy grail. Our DCF assessment also reflects this fact. Companies not able to grow its revenue to the US$15-20bn a year range with gross margin north of at least 70% will have difficulty to pay for its OPEX to arrive a positive NPV;

Chinese biotech/biopharma must learn to sell drugs outside of US to avoid sanction and outside of China to make profit.

- **Selling drugs worldwide will be more important than selling drug at home**: The reason we view BGNE as the only investible biotech stocks in China is because its revenue and R&D footprint are both global. Its R&D spending is the sum of our next six coverage names combined, yet its drugs are receiving recognition by FDA/EMA/PMDA like. We believe with the eventual US blockade on biotech similar to the one on semiconductor, the ability to sell outside of US and outside of China will be key for Chinese biotech/biopharma's. However, FDA is still the global gold standard of pharmaceutical management. Outside of BGNE, the number of clinical trials conducted by Chinese biotech's abroad are worryingly low. Chinese innovative drug must win US FDA if they cannot win US Congress. China's participation in global drug regulatory bodies like ICH is taking up the initial steps;

- **Choosing the right battlefield and conserving the bullets are still winning strategies**: Innovative drug is different from semiconductor in that it doesn't rely on a single thread of supply chain, which US and its Asia allies have dominated. Leap frog in biotech can happen

in many subfields. Akeso and RemeGen have focused on BsAb and ADC as battlefields and have won. Legend Bio and CARsgen are leading globally in CAR-T. RemeGen's OPEX is the smallest of all stocks we cover and was only 1/15 of BGNE in 2021 and thus can afford more missteps or bad lucks. The best biotech must balance cost with speed of discovery. The best biopharma must excel in R&D, sales and license-in/out. The race of biotech is a marathon. The race of biopharma is a triathlon;

There are still a constant stream of Chinese biotech's going public, in new fields like gene therapy and mRNA vaccines, for example.

- **Over-crowding in development does exist, but biotech's failure rate will always be high**: We examined the competitive landscape of major biological segments. While competition is indeed heating up, the quality of competition cannot be taken for granted. China, in general, suffers a lack, not an abundance of medical research talents. Our BUY-rating companies have at least a year lead against their nearest domestic peers. The only area we believe over-crowding may play a part in valuation is CAR-T, which is still early stage and suffers critical technology and business model deficiencies. Lastly, we also view the expansion of the number of biotech's investible as a welcoming development. China has its entries in new fields like gene therapy and mRNA vaccines, to name a few;
- **Pricing pressure in China will remain but there are also silver linings in generic substitution**: The existing of NDRL has permanently damaged the attractiveness of China's innovative drug industry. NDRL will stay because China is underfunded in its pension and health insurance funds and China's state healthcare complex has the dominance to do it. However, there is silver lining. >80% of drugs sold in China, the world's 2nd largest pharmaceutical market, is now generic. There is a country wide consensus to replace it with innovative drugs but the question is who and how. This opportunity is available to global pharma/biopharma/biotech's as well but their drug cost must come down. Domestic companies may benefit more;

China's pension and healthcare insurance are short historied, thus the pressure to reach fully funded point is the greatest in the beginning.

- **The US and China markets for innovative drug will converge**: Today in pharmaceuticals, China is price sensitive while US is price insensitive. China is low-cost producer and US is high price consumer. We believe the direction is for US to be more price sensitive while China becoming less price sensitive, once its funding gap is alleviated. There is opportunity for some Chinese biotech/biopharma/pharma's to break into global top 20's along this process, in our opinion;
- **Reverse talent drain is also a major risk**: 60-70% of Chinese biotech's are founded by overseas returnees. An exclusivity campaign on Chinese Americans can deal the biggest blow on China's biotech industry, which combined with a demand choke can throw the industry off balance;
- **The spot for global 20 is very few**: Given the above, we believe there is the possibility of only one to three spots for Chinese biotech/biopharma/pharma's to break into global 20. BeiGene is our best bet.

COVID and beyond show aspiration and reality

The COVID-10 pandemic led two vaccine companies into the global pharmaceutical's top 20, suggesting upward mobility in this space is still possible. But over the longer horizon, few biotech's have shown staying power. China, for its own social security cost and industry policy purposes, has made the nurturing of a competitive innovative drug industry a national priority. It has been very successful so far. Chinese innovative drug developers, in the case of PD-1/L1 anti-cancer drugs, have shown global potential as a price deflator. Despite obstacles, we conclude their competency is real and will likely climb higher in the global value chain in the coming decade.

Breaking into global top tier is a doable but tough business

In 2021, BioNTech (BNTX US, NR) and Moderna (MRNA US, NR) broke into the global pharmaceutical top 20 (Exhibit 23). Adding Gilead (GILD US, NR) and Amgen (AMGN US, NR), biopharmas now contribute 4 out of the global top 20. In China, Kexing Biopharm (688136 CH, NR), the maker of Sinovac vaccine, also saw its revenue rose from US$246mn in 2019 to US$19.4bn in 2021 (Exhibit 24), but did not get recognized as one of the global 20.

Over the past four decades only four biotech companies successfully break into global top 20 and become biopharmaceuticals (biopharma).

Exhibit 23. Founding time of Top 20 global pharmaceutical companies and their revenues

Rank	2019	2020	2021	2021 list	
				Established Time	2021 revenue (US$ bn)
1	J&J	J&J	Johnson & Johnson (J&J)	1886	93.8
2	Roche	Roche	Pfizer	1849	81.3
3	Pfizer	Novartis	Roche	1896	68.7
4	Novartis	Merck	AbbVie (Abbott Lab)	1888	56.2
5	Merck	AbbVie	Novartis (Ciba-Geigy/Sandoz)	1857	51.6
6	GSK	GSK	Merck	1891	48.7
7	Sanofi	BMS	Bristol Myers Squibb (BMS)	1887	46.4
8	AbbVie	Pfizer	GlaxoSmithKline (GSK)	1715	43.6
9	Takeda	Sanofi	Sanofi (Aventis/Hoechst/RP)	1863	44.7
10	Bayer	Takeda	AstraZeneca (AZ)	1913	37.4
11	BMS	AZ	Takeda	1781	31.6
12	AZ	Bayer	Eli Lilly	1876	28.3
13	Amgen	Amgen	Bayer	1863	28.2
14	Gilead	Gilead	Gilead Science	1987	27.3
15	Eli Lilly	Eli Lilly	Amgen	1980	26.0
16	BI	BI	Boehringer Ingelheim (BI)	1885	24.4
17	Novo	Novo	Novo Nordisk (Novo)	1923	22.4
18	Teva	Teva	**BioNTech**	2008	22.4
19	Allergan	Biogen	**Moderna**	2010	18.5
20	Biogen	Astellas	Viatris (Mylan/Upjohn)	1886	17.8

Source: Fierce Pharma, Blue Lotus, (2022/10/21)

The emergence of COVID-19 vaccine makers shows global pharmaceutical is still an R&D driven growth industry. But such outcomes are exceptions rather than rules. Both BioNTech and Moderna are expected to lose about half of their revenues by 2023 (Exhibit 24). With COVID-19 increasingly becoming a "big flu", the need to have regular vaccine shoot has become moot. Whether Sinovac really broke into global 20 has also become irrelevant.

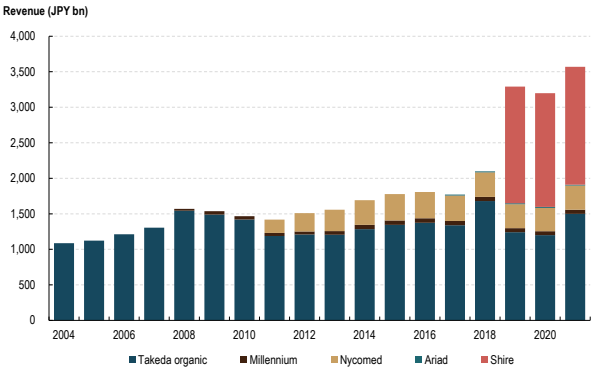
R&D has diseconomy of scale but regulatory, sales and manufacturing of drugs have economies of scale.

Exhibit 24. From nowhere to global 20 in 2021 (revenues)

(US$mn)	2017	2018	2019	2020	2021	2022E	2023E
BioNTech	69	151	122	550	22,430	17,033	10,360
Moderna	206	135	60	803	18,471	21,901	10,173
Sinovac	174	230	246	511	19,375	NA	NA

Source: BioNTech, Moderna, Sinovac, Blue Lotus (2022/10/21)

Exhibit 25. Acquisition's contribution to Takeda



Source: Takeda, Blue Lotus (2022/10/21)

Throughout the history of pharmaceuticals, only Amgen and Gilead have broken into the top rank and stayed, thanks to their blockbuster drugs treating Arthritis (关节炎), Neutropenia (嗜中性白血球减少症), Anemia (贫血), Hepatitis (肝炎) and AIDS. Genentech and Biogen have broken in but then failed. The ranks of top global pharmaceuticals companies are surprisingly stable. For 9 years from 2013 to 2021, a total of 24 pharmaceutical companies have shown up for all the list for the global top 20, a redundancy ratio of 98% (*Source: Fierce Pharma*).

In the past decade, 98% of the global top 20 pharmaceutical companies list are the same.

Managing big infrastructure fixed cost and innovation are required

Such, in our view, illustrates the nature of the innovative drug business. To maintain R&D, regulatory and sales a company needs incur a huge amount of fixed cost, especially large in today's globalized market. To maintain this level of fixed cost the company needs to have at least one, possibly several blockbuster drugs, preferrable first to the market to beat the competitors making similar clinical claims, in addition to generic drug makers waiting to clone the invention once the patent expires. An effective fixed cost operation, on the other hand, can be "rented out" to lower the point of breakeven. It can break-the-tie against a rival when other factors are equal.

While R&D of drugs displays diseconomy of scale, clinical trials, sales marketing and manufacturing display economy of scale. An innovative drug company must excel in both areas of the business at different phase of their life cycles. Hence are the difficulties.

To continually grow, a drug company needs to master different skills at different phase of their business.

As Exhibit 23 shows, most of the global top 20 were founded in two centuries ago in the era of chemical and small molecule drugs. The advent of large and very large molecule drugs, the so-called biopharmaceuticals and biologics, has ushered in new entrants in the global pharmaceutical landscape, making the Amgen's and Gilead's possible.

Acquisition can help patch the divided in skill

Smart acquisition strategy is also vital to take advantage of the R&D pipeline of the startups. Exhibit 25 showed a simplified illustration of acquisition's contribution to Takeda's top line, assuming flat revenue for the acquired entities. Without acquisitions Takeda's revenue would have been flattish in the past decades. Takeda's reputation as an accommodative business partner, built as a result of its successful joint venture with Abbott Laboratories (TAP Pharmaceuticals) from 1977 to 2008, helped it forming a reputation as a consolidator.

The US China rivalry in semiconductor today is a foreplay of the same in innovative drugs a decade later.

China has strategy to build a world class innovative drug industry

China's reform on its innovative drug industry started in 2015, together with sweeping reforms on drug distribution, pricing, insurance and payment. Encouraging the development of a world class innovative drug industry is vital for lowering the end price for China's aging population. It also has military and diplomatic implications as the breakout of US-China relations and the outbreak of COVID-19 pandemic have shown.

Seven years later China has formed the broad outline of a hospital-pharmacy-insurance healthcare complex that is unseen anywhere in the world. Such a complex controls 71% of hospital beds, 78% of healthcare workers, 65% of pharmacy revenues and 95% of health insurance premiums (75% national + 20% commercial by SOE). Armed with the success of such complex, Chinese government has an unparalleled war chest to implement its strategy, constituting both lowering the medical cost for the nation and nurturing a globally competitive innovative drug industry, in our view.

For details on China's reform to transition from a Beveridge Model to a Bismarck/Single Payor Hybrid Model, please refer to our healthcare information system sector initiation <*Early state calls for prudence*>.

Exhibit 26. Drug evaluation submission and approval rates, China, US and EU

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022YTD
Submissions										
Accelerated track										
China CDE					51	101	90	188	278	101
US FDA	43	59	101	48	94	133	108	79	108	61
EU EMA	2	6	9	11	6	9	0	0	3	0
Standard Track										
China CDE	-	-	-	50	60	150	117	267	177	160
US FDA	243	215	199	201	254	211	199	180	151	171
EU EMA	67	62	73	82	72	78	66	86	91	63
Approvals										
Accelerated track										
China CDE	-	-	-	-	30	36	32	67	99	36
US FDA	34	47	81	38	75	106	86	63	86	49
EU EMA	1	4	6	7	4	6	0	0	2	0
Standard Track										
China CDE	-	-	-	7	9	72	56	128	85	77
US FDA	194	172	159	161	203	169	159	144	121	137
EU EMA	62	50	61	48	66	61	52	67	71	49

Source: NMPA, FDA, EMA, Blue Lotus (2022/10/21)

Accelerated Track and Conditional Approval are keys to leapfrog

In 2021, China (1) approved more drugs under the Accelerated Track than under the Normal Track and (2) approved more drugs under Accelerated Track than US. The same is not true for drugs approved under the Standard Truck, even though it also showed remarkably growth. This suggests China has heavily relied on conditional approval to fast track its drug discoveries. This scenario has gone so far that in October 18, 2022, Roche China issued a statement accusing NMPA of approving a drug, made by CSPC (1093 HK, NR) that breaches another NMPA approved drug Baloxavir Marboxil (*Xofluza*) made by Roche (ROG SW, NR).

The biotech bull market in the last five years had to do with loose approval by CDE/NMPA.

Such action, in our view, reflects the general trend of reversal in 2022, a year which China likely approved fewer drugs than US in both Accelerated and Standard Track and accelerated the approval of imported drugs, signalling CDE/NMPA is tightening the standard and raising the bar (Exhibit 26).

Accelerated approval of life saving drugs is a global coordinated action

FDA launched Accelerated Track drug approval mechanism in 1992. Other mechanisms like Priority Review, Fast Track and Breakthrough Therapy were added in the same year or after. The key and the controversy to Accelerated Track is it allows drug companies to use surrogate end points at clinical trials to act as a basis for Conditional Approval. Such practices were further legislated in the 2012 <*FDA Safety Innovation Act*>.

While many disagree to equate conditional approval to approval based on surrogate clinical end points. The net outcome is the same: drugs hitting the market before full data is known.

The original purpose of Accelerated Track is to expedite the approval of life-critical cancer and HIV treating drugs using the latest biologics discoveries. Such regulatory thought was also followed by EU's European Medicine Agency (EMA) and China's Center of Drug Evaluation (CDE). Exhibit 27 shows China's 4 mechanisms of accelerated drug approval: (1) Conditional Approval (附条件批准上市), (2) Priority Review and Approval (优先审评审批), (3) Breakthrough Therapy and Drugs (突破性治疗药物), (4) Special Approval (特别审批), as stipulated in the January, 2020 <*Provisions of Drug Registration*> (《药品注册管理办法》).

But backpedalling now seems in order

However, there has been constant debates and reviews about the possible abuse of the Accelerated Track programs. Technically, an Accelerated-Track-approved drug shouldn't represent a water down of the clinical requirement. The approved drug should withdraw as quickly as possible if end point clinical data proved otherwise from the surrogate. But in reality, both offenses of crafty clinical design and slow withdrawal under unfavourable data occurred. FDA has always disputed the equivalence of surrogate end point to conditional approval, we hold the view that the net outcome is the same. The EU terminology of Conditional Marketing Authorization as the equivalent mechanism to Accelerated Approval proved the point. It is a conditional approval.

Abuse of the accelerated approval/conditional approval mechanism has become a concern. If so, China certainly has more of it.

In 2021, the Accelerated-Track approval of Biogen's Alzheimer-treating drug *ADUHELM* led to the resignation of three FDA panel members. In April 2022, Biogen withdrew *ADUHELM* from EMA. Also in April 2022, The Centres for Medicare & Medicaid Services (CMS) refused to reimburse *ADUHELM* in the US.

We believe it is likely the Accelerated Track approval process will get increasingly scrutinized in the US, which will make the approval more conservative. Such policy inclination will also impact China because the abuse is more widespread. We are already seeing statistics of slowdown in conditional approval in 2022 and acceleration in approval of imported drugs. We also saw CDE of NMPA to step up the drafting of guidelines and standard operating procedures. But we believe after the

We believe a slowdown in approval speed is in order but it will likely not last long.

consolidation we will continue to see fast approval of drugs to facilitate the development of innovative drugs in China.

Exhibit 27. Drug evaluation submission and approval rates, China, US and EU

US	Key criteria	Key benefit	EU Equivalent	China Equivalent
Fast Track	Facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need	(1) More frequent communication w/ FDA, (2) Eligible for Accelerated Approval or Priority Review, (3) Rolling review	PRIME	NA
Accelerated Approval	Expedite drugs for serious conditions that fill an unmet medical need	Allow FDA to approve drugs based on surrogate or intermediate end point with full clinical end point result available later	Conditional Marketing Authorization	附条件批准上市
Priority Review	Drugs that can be significant improvements in the safety or effectiveness of the treatment when compared to standard applications	FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review)	Accelerated Assessment	优先审评审批
Breakthrough therapy	Drugs that treat a serious condition or can bring substantial improvement over available therapy on a clinically significant endpoint(s)	(1) All Fast Track designations plus intensive coaching, (2) Clinically significant endpoint	Advanced Therapy	突破性治疗药物
Orphan drug	Prevent, diagnosis and treatment of rare disease	(1) Tax credits for clinical trials, (2) 7 year exclusivity after approval	Orphan Medicines	NA
Emergence Use Authorization	Help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats including infectious diseases	Authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency	Conditional Marketing Authorization	特别审批

Source: CDE/NMPA, FDA, EMA, Blue Lotus (2022/10/21). CDE is a division of NMPA, which is the new name for CFDA after Sept. 2018

PD-1/L1 market left with both seeds of hope and hubris of pride

China achieved domestic substitution of oncology drugs PD-1/L1 at the expense of domestic drug maker's profitability.

Taking advantage of the big molecule biologics as a new drug development platform, regulators around the world encouraged drug development by biotech start-ups. China is no exception. Fierce competition occurred in target duplication and indication overlap especially in the field of PD-1/L1 and cell therapy.

Exhibit 28 shows PD-1/L1 drug approved for sale in China, totalling 11 domestic and 4 imported as of October, 2022, among which 4 have been selected for National Drug Reimbursement List (NDRL), the collective bargaining program of China's state healthcare complex. All 4 imported PD-1/L1 drugs have walked out of the NDRL negotiation, opting for trying their luck in retail. We noted that NMPA has continued to approve PD-1/L1 drugs in 2021-2022 while import applications has largely dried up. We found at least three currently selling PD-1/L1 drugs elsewhere, *Bavencio* (Merck), *Libtayo* (Regeneron) and *Jemperli* (GSK), aren't available and aren't in approval in China (Exhibit 29).

China 's PD-1/L1 drugs did make curing cancer affordable for many. Imported PD-1/L1 drugs are sold in China at about half the price in US while domestically developed PD-1/L1's are further 90%+ off.

We count an incomplete list of 29 PD1/L1 drugs under clinical trials as of October, 2022, among which 12 were from Chinese biotech/biopharma companies. As the development of PD1/L1 passing its commercialization stage, many biotech/biopharmas have turned to alternative targets such as TIGIT (T-cell immunoglobulin and ITIM domain), CLTA-4 (Cytotoxic T-lymphocyte-associated Protein 4) and LAG-3 (Lymphocyte-activation Gene 3), HER-2 (Human Epidermal Growth Factor Receptor 2) and the combination of these with PD-1/L1, as well BsAb (Bispecific Antibody) which combines two biotargets in one.

What domestic PD-1/L1's have accomplished is affordability

National Healthcare Security Administration (NHSA) uses NDRL to quickly lower the price of PD-1/L1 drugs, together with other drugs, by 60-90%. This is made possible by the sheer number of PD-1/L1 drugs approved by NMPA. Up till now FDA only approved 7 PD-1/L1 drugs, with the first

approval took place in 2014 (*Keytruda* by Merck and *Opdivo* by BMS). But up till now CDE of NMPA has approved 15, 11 domestic and 4 imported, with the first approval taking place in December of 2018 (Toripalimab by JUNSHI).

Exhibit 28. Chinese PD-1/L1 on market

Clinical name (trade name)	Developed by	Indication	Date of approval	NRDL
Toripalimab 特瑞普利单抗（拓益）	JUNSHI (1877 HK)	NPC (鼻咽癌), Melanoma (黑色素瘤)	2018.12	√
Sintilimab (Tyvyt) 信迪利单抗 (达伯舒)	Innovent (1801 HK)	Lung & liver cancer, Lymphoma	2018.12	√
Camrelizumab 卡瑞利珠单抗 (艾瑞卡)	HENGRUI (600276 CH)	Lung & liver cancer, NPC, UCC	2019.5	√
Tislelizumab 替雷利珠单抗 (百泽安)	BeiGene (BGNE/ 688235 CH)	Lung & liver cancer, Lymphoma (淋巴瘤), UCC (尿路上皮癌)	2019.12	√
Penpulimab 安尼可	AKESO/SINO (9926 HK/1177 HK)	Lung & liver cancer, NPC	2021.8	
Zimberelimab 誉妥	Gloria/Wuxi (002437 CH/ 2269 HK)	Cervical & gastric cancer (宫颈癌, 胃癌)	2021.8	
Envafolimab 恩唯达	Alphamab (9966 HK)	Solid tumor & hepatitis B (乙肝)	2021.11	
Sugemalimab (Cejemly) 舒格利	CStone (2616 HK)/ Pfizer (PFE US)	Non-small cell lung cancer (NSCLC)	2021.12	
Serplulimab 汉斯状	Henlius (2696 HK)	Solid tumor	2022.3	
Candonilimab 开坦尼	AKESO	Cervical cancer	2022.6	
Pucotenlimab 普佑恒	LEPU/Hanx (2157 HK)	Solid tumor	2022.7	
Pembrolizumab (*Keytruda*) 可瑞达	MSD (MRK US)	Lung & liver cancer, Melanoma, CRC	2018.7	
Nivolumab (*Opdivo*) 欧狄沃	BMS (BMY US)	NSCLC, CRC (结直肠癌), Glandular (腺癌)	2018.6	
Durvalumab (*Imfinzi*) 英非凡	AstraZeneca (AZN LN)	NSCLC	2019.12	
Atezolzumab (*Tecentriq*) 特善奇	Roche (RO SW)	Lung & liver cancer	2020.2	

Source: CDE, Blue Lotus (2022/10/21)

Exhibit 29. PD-1/L1 out of China + under development

Clinical/target (trade name)	Developed by	Indication	Approval date /Clinical phase
Avelumab (Bavencio)	Merck (MRK US)	Skin cancer, kidney cancer	2020.6
Cemiplimab (Libtayo)	Regeneron (REGN US)	Skin cancer	2021.2
Dostarlimab (Jemperli)	GSK (GSK LN)	Adv. Endometrial cancer	2021.8
Geptanolimab (GB226)	GENOR (6998 HK)	Peripheral T Cell Lymphomas	III
AK112	AKESO	Lung cancer	III
IBI-322	Innovent	Solid tumor	II
IBI323	Innovent	Advanced tumor	I
HX009	Hanxbio (翰思)	Liquid/solid tumor	II
QL1706	Qilu (600756 CH)	Cervical cancer	III
QL 1604	Qilu	Solid tumor	II
SHR-1701	HENGRUI	Gastric, Glandular	II
KN046	Alphamab (9966 HK)	NSCLC	II
ES101	Inhibrx/Elpiscience	Private	I
EMB-02	Epimab (岸迈)	Private	I
EMB-09	Epimab	Private	I
Tebotelimab (MGD 013)	MacroGenics (MGNX US)/ZLAB	Solid Tumors & Heme Malignancies	II
Lorigerlimab (MGD-019)	MacroGenics	Melanoma, MSS CRC (结肠癌), Lung	II
RG-6139 (RO-7247669)	Roche (ROG SW)	Solid tumor	II
RG-6279	Roche	Solid tumor	I
PF-06801591	Pfizer	Bladder cancer	III
AZD-2936	AstraZeneca	Solid tumor	I
AZD-7789	AstraZeneca	Solid tumor	I
MEDI-5752	AstraZeneca	Adv. Renal Cancer	II
Vudalimab (XmAb-717)	Xencor (XNCR US)	Prostate, Adv. Gyn. Malignancies	II
XmAb-104	Xencor	Colorectal, NSCLC	I
MCLA-145	Merus (MRUS US) /Incyte (INCY US)	Solid tumor	II
ONO-4685	Ono (4528 JP)/Merus	T-cell Lymphoma	I
Duobody (GEN-I046)	Genmab (GMAB US)/ BioNtech (BNTX US)	Solid tumor, Lung	II
FS-118	F-Star (FSTX US)/ MSD	Head & neck, lung	II
FS-222	F-Star/MSD	Low tumor	I
ABL-501	ABL Bio (298380 KS)	Solid tumor	I
ABL-503	ABL Bio	Solid tumor	I

Source: CRI, Blue Lotus (2022/10/21)

Thanks to this overwhelming supply, Chinese PD-1/L1 drug makers enthusiastically embraced the NDRL in order to enter the state-owned hospital pharmacy channel, ~65% of China's total Rx drug distributed. Making it to the NDRL typically leads to first year sale jump but subsequent years of stagnation or even decline.

What NDRL and redundant effort of PD-1/L1 R&D have successfully accomplished is to make cancer curing more affordable. As Exhibit 30 shows, global pharma's already priced their PD-1/L1 in China 45-50% below their US prices before domestic PD-1/L1 hit the market. Nevertheless, after NDRL price cuts Chinese PD-1/L1 drugs are a further 90%+ discount from prior. As shown in Exhibit 30, the average prices of Chinese PD-1/L1 drugs before NDRL were already 47% of their imported counterparts in China and 26% in US. After NDRL, they dropped to 7.5% and 4.2%. China has reduced the out-of-pocket cost for cancer treating to US$1,500-5,000 a year.

NDRL price reduction cost gross margin to temporarily drop. But with the exception of JUNSHI, all recovered quite quickly.

Exhibit 30. PD-1/L1 drug price in China and US

(US$)	Maker	Price/yr. before NDRL	Price/yr. after NDRL	US price
Domestic developed				
Camrelizumab	HENGRUI	US$51,389	US$7,658	NA
Sintilimab	Innovent	40,686	5,606	NA
Tislelizumab	BEIGENE	55,480	7,527	NA
Toripalimab	JUNSHI	24,183	6,422	NA
Imported				
Keytruda	Merck	US$93,009	US$93,009	US$171,139
Opdivo	BMS	88,217	88,217	194,532
Tecentriq	Roche	85,130	85,130	168,232
Imfinzi	AZ	95,878	95,878	120,559
Domestic/Imported		47%	7.5%	26%/4.2%

Source: HENGRUI, Innovent, BEIGENE, JUNSHI, Drugs.com, Blue Lotus (2022/10/21). Assuming 60kg patient. Imported drug has various charity discount which can lower the price by up to 50% if meeting certain income standards.

Exhibit 31. Gross margin before and after NDRL

	1H19	2H19	1H20	2H20	1H21	2H21	1H22
BGNE	NM	NM	76%	78%	80%	85%	83%
Innovent	88%	79%	78%	90%	90%	90%	88%
JUNSHI	87%	89%	89%	69%	(21%)	(615%)	26%
HENGRUI	83%	80%	88%	75%	87%	73%	83%

Source: BGNE, Innovent, JUNSHI, HENGRUI, Blue Lotus (2022/10/21)

Exhibit 32. Revenue comparison of PD-1/L1 drugs

US$ mn/Rmb mn	2019	2020	2021
Toripalimab (JUNSHI) in China in Rmb	774	1,003	412
Sintilimab (Innovent)	1,016	2,289	2,801
Camrelizumab (HENGRUI)	1,425	6,077	4,141
Tislelizumab (BeiGene)	0	1,118	1,647
China sales of dom. dev'd PD-1/L1 in Rmb	Rmb3,215	10,487	9,001
In US $ mn	**US$465**	**1,555**	**1,394**
Keytruda (Merck) in non-US	4,768	6,028	7,421
Opdivo (BMS)	2,860	3,047	3,321
Tecentriq (Roche)-USD	704	1,245	1,760
Imfinzi (AstraZeneca)	428	858	1,166
Non-US sales of imported PD-1/L1 in US$ mn	**US$8,760**	**11,178**	**13,668**

Source: JUNSHI, Innovent, HENGRUI, BEIGENE, Merck, BMS, Roche, AstraZeneca, Blue Lotus (2022/10/21)

Exhibit 33. NMPA indications approval for China PD-1/L1

Drug	Camrelizumab	Sintilimab	Tislelizumab	Toripalimab
Maker	HENGRUI	Innovent	BeiGene	JUNSHI
2018	-	-	1	1
2019	1	1	1	-
2020	3	-	-	-
2021	4	2	4	3
2022 YTD	0	2	3	2
China total	8	5	9	6
Pending				
NMPA	0	0	2	0
FDA	2	Failed	2	1
EMA	1	2	2	1
Global total	11	7	15	8

Source: CDE (NMPA), Blue Lotus (2022/10/21)

From the investor's point of view, this is certainly not a good news. Thanks to NDRL, China sales of PD-1/L1 drug made by Chinse innovative drug developers reached ~US$1.4bn in 2021, shrinking 10% YoY after just one year on the market (Exhibit 32). This had made the small China sales in the global pie eventually smaller. In 2021, the non-US sales of the 4 global PD-1/L1 drugs reached US$13.7bn, up 22% despite a strengthening dollar. China typically constitutes <10% of revenues of global pharma's so the loss of sales in China doesn't impact their top line. But our channel check did suggest the sales of imported PD-1/L1 drugs were affected in China. What Chinese innovative drug developers have demonstrated was the remote potential of deflating the future revenue potential of the global market.

What China's PD-1/L1 effort has demonstrated is China's ability and potential to deflate global innovative drugs industry.

Going forward, we expect domestically developed PD-1/L1 drugs to resume growth in revenues as more indications are approved. BGNE's Tislelizumab received 9 indications, 3 in C1H22, 4 in 2021 and 1 each in 2019 and 2018, driving strong revenue growth in C1H22. HENGRUI's Camrelizumab received 8 indications, none in C1H22, 4 in 2021 and 4 in 2020. Innovent's Sintilimab received 5 indications, 2 in C1H22, 2 in 2021 and 1 in 2019, thereby driving a rebound in its C1H22 top line. JUNSHI's Toripalimab received 5 indications, 2 in C1H22, 3 in 2021 and 1 in 2018 (Exhibit 33). We believe a rebound in Toripalimab is also likely.

BEIGENE and Innovent saw PD1/L1 revenue growth in C1H22. thanks to new indication approvals. But total indications are far below global peers.

For comparison, *Keytruda* (Merck) is approved for 30 indications by FDA, 21 by EMA, 16 by PMDA and 8 by NMPA, totaling 75 in US, EU, Japan and China alone (*Source: FDA, EMA, NMPA, PMDA*).

Several reasons contributed to *Keytruda*'s continuing strong sales in China and globally.

- **Indications**: As one of the oldest approved PD-1/L1 it was approved for the widest indications among peers. Although *Keytruda* was only approved for 8 indications in China, it doesn't deter Chinese doctors from prescribing per FDA approvals (off the label);
- **Safety**: the toxic and side effects of *Keytruda* are well known;
- **Commercial insurance coverage**: *Keytruda* (Merck), *Opdivo* (BMS) and *Tecentriq* (Roche) were included in Shanghai's Huimin Insurance Program (惠民保), a state-commercial hybrid insurance program test-watered by many local governments;
- **Affluent population and stereotyping:** Imported PD-1/L1 has historically targeted China's affluent population, which can still afford imported. Some Chinese also holds less trust on domestically developed drugs.

China's underdeveloped commercial health insurance can also support the price of imported drugs in the future.

Non-inferiority vs. cost benefit drive Chinese PD-1/L1 overseas

Chinese PD-1/L1 developers forged global distribution partnerships. In dealing with FDA the main selling point is the lowering the cost of treatment. However, they also face the challenge of non-inferiority (NA), which means a new experimental drug should not be unacceptably less efficacious than an active control treatment already in use. The choice of active control treatment already in use is tricky. Earlier PD-1/L1 has the liberty of choosing chemotherapy but later ones must choose the already approved PD-1/L1.

Cost benefit argument works in China but doesn't work in US regulatory decisions.

PD-1/L1 is strategic.

The non-inferiority doctrine is also dependent on the indication sought after and possible combination with other drugs. PD-1/L1 is known for poor Overall Response Rate (ORR), good Progression Free Survival (PFS) and good Overall Survival (OS). It has broad spectrum and low toxicity, which are tied to PD-1/L1's mechanism of action. Combinational use with other oncology drugs is an effectively way to improve PD-1/L1's ORR. Therefore, many Chinese innovative drug developers view PD-1/L1 as strategic that must win despite a fierce competitive environment.

Currently, with the exception of Innovent/Eli Lilly's Sintilimab, all three selling domestically developed PD-1/L1 are expected to pass FDA approval. Outside the selling 4, Serplulimab from Henlius (2696 HK, NR) is likely to submit and receive FDA approval as well.

With the exception of Innovent's Sintilimab, all leading PD-1/L1 from China will likely get FDA approval in 2023.

- **Innovent/Eli Lilly was hit with FDA rejection**: Innovent partnered with Eli Lilly (LLY US, NR) in August 2021. LLY made a US$200mn upfront payment for ex-China right to sell Sintilimab (*TYVVT*) and up to US$825mn for milestone payments. In February 2022, FDA rejected the application of Sintilimab on the ground it didn't contain US ethnic population in its clinical trials. We notice that Sintilimab has submitted global clinical trials for Esophageal Squamous Cell Carcinoma due to complete in December 2023-June 2025 (*Source: Clinicaltrials.gov*);

- **BGNE/Novartis delayed due to COVID but likely**: In January 2021, Novartis (NOVN SW) forged an ex-China, developed country distribution partnership with BGNE for Tislelizumab, in which BGNE received an upfront payment of US$650mn, regulatory and sales milestone fees up to US$1.55bn. In July 2022, FDA delayed its approval decision on the ground of difficulty to travel to China to inspect production onsite. We understand there is still a high chance Tislelizumab might be approved. In July 2017, BGNE first licensed Tislelizumab to Celgene. In June 2019, Celgene sold the rights back to BGNE and paid US$150mn penalty after it was acquired by BMS, which produces rival drug *Opdivo*;

- **JUNSHI/Coherus wait for decision at year end after resubmission**: On February 1, 2021, JUNSHI signed a North American distribution agreement worth US$1.11bn with Coherus Bioscience (CHRS US, NR) for Toripalimab. On July 6, 2022, JUNSHI and Coherus announced that FDA has accepted the resubmission of application for the drug for Biologics License Application (BLA). FDA's decision is due in six months of time, provided an on-site inspection to China can be arranged. Although Toripalimab's client trial is also predominantly Chinese, it might be helped by the fact that its indication in Nasopharyngeal Carcinoma (鼻咽癌) is more sought after in the US than Innovent/Eli Lilly's Sintilimab. Toripalimab's EMA submission is made by TMC Pharma Services;

- **HENGRUI soon to apply for FDA approval for a combination treatment**: On May 12 2022, HENGRUI announced a good result of its global phase III trial of Camrelizumab and VEGFR inhibitor Apatinib (Rivoceranib), for liver cancer, beating Bayer's *Nexavar* as placebo. Currently HENGRUI partners with Elevar Therapeutics (private) for the distribution of Rivoceranib in North America. Camrelizumab's EMA filing was submitted by Medvir AB (MVIRB SS, NR). If approved, Camrelizumab+Rivocertanib will compete against Roche's Tecentriq+Avastin. In May 2020, HENGRUI licensed Camrelizumab to Crystal Genomics (083790 KS, NR) for commercialization in South Korea for US$88mn in total (*Source: PharmCube*);

- **Gloria (002437 CH, NR) sold Zimberelimab's ex-China rights** to Arcus Bioscience (RCUS US, NR) for US$816mn in total in August 2017 (*Source: PharmCube*). Arcus now has several Phase II trials underway in the US.

Chinese PD-1/L1 has proven to be a global deflation force

Imported PD-1/L1 shall see their market share shrink but impact on their overall financial is minuscule because their contribution to global sales is small to begin with.

The emergence of domestically developed PD-1/L1 brought down imported price of PD-1/L1 by ~50% and NDRL further reduce the price by 60-90%. As these PD-1/L1's going through FDA approval, their efficacy and toxicity profile become increasingly known. Some, like HENGRUI's Camrelizumab, is known for having side effects like causing Capillazy Hemangioma (毛细血管瘤), but most others are proven safe so far.

According to our channel check, *Keytruda* sales in China was flat in 2021 at Rmb3.5-4bn (US$ 526-602mn), less than 0.8% of Keytruda's non-US sales but already the No.1 selling PD-1/L1 in China. With domestically developed PD-1/L1 selling through NDRL, we expect *Keytruda* sales to suffer 15-25% decline in 2022.

Chinese developed innovative drugs have shown the potential to deflate global drug prices.

According to our channel check, *Opdivo* sales was still growing in 2021 and 2022 from a low base with more indication approvals. But with Sintilimab's (Innovent) approval for Gastric Cancer in June 2022, one year after *Opdivo*'s same approval, we expect *Opdivo*'s sales to decline in 2022 from ~Rmb1bn (US$150mn) in 2021.

The question is what will happen if in the next round of competition, Chinese innovation drug developers shorten their development and trial gap with the global pharma's? Afterall, drugs aren't fashion bags. Drug has no brand value, except efficacy, safety and price.

Getting FDA approval≠US sales, but still matters a lot

FDA will take on global responsibilities in evaluating innovative drugs from China, which come with drastically lower price tag than before.

We believe Chinese innovative drug developers will not sell their drugs at the same low price as in China after they get approval from FDA. Hiking prices can make up for the profit lost, repair share prices and ease entry to other developed market without irking the medical community.

However, given >1/3 of US healthcare expenditures were paid by commercial insurers and 3/4 of US prescription drugs were dispensed by retail pharmacies, getting FDA approval doesn't mean getting the drugs sold in the US.

The relationship between US healthcare complex and global pharma/biopharma is a company-to-company relationship. It won't be rocked by a single drug.

Although the US healthcare complex aren't as dominant as that in China, it is the place where healthcare complex originated. Vertical integrations of hospitals, pharmacies and insurers took place a decade ago. In 2011, United Healthcare (UHC US, NR) formed Optum, which now covers pharmacy (OptumRx), hospital service (OptumHealth) and digital health (OptumInsight). Along the way UHC acquired close to a dozen companies. In 2017, CVS (CVS US, NR) merged with insurer Aetna (AET US, NR). In 2018, insurer Cigna (CI US, NR) acquired pharmacy Express Scripts and insurer Humana (HUM US, NR) acquired pharmacy Kindred. Walgreens Boots (WBA US, NR), on the other hand, horizontally integrated Rite Aid (RAD US, NR), Alliance Boots and PharMerica. Drugs from Chinese innovative drug developers won't sell in the US market unless they win the support of the US commercial insurers and pharmacies, which form complex relationships with major pharma's and biopharma's. The relationship between US healthcare complex and global pharma/biopharma is a company-to-company relationship. It won't be rocked by a single drug, no

matter how big it is, let alone no drug from Chinese innovative drug developers has ever come close to the US$1bn a year blockbuster line.

Still, we believe getting FDA approval for innovative drugs from China carries a lot of meanings.

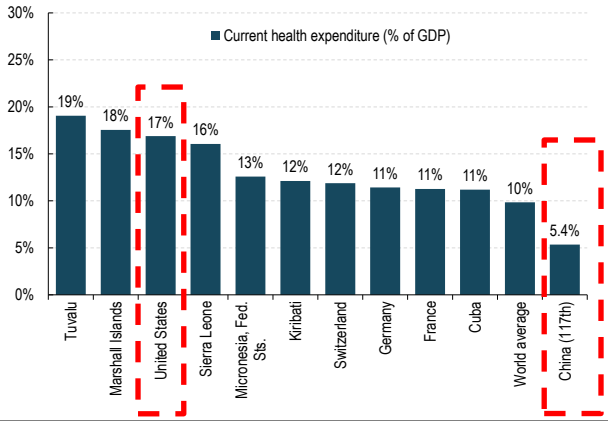
In our view, two questions will be outstanding after these drugs received FDA approval

- **How much profit will be deemed enough by these Chinese developers?** We believe it really depends on (1) how sustainable the gene revolution we are in and (2) how organized China's industry policy of nurturing the innovative drug industry will be. If the fundamental competency of Chinese developers is quality development at low cost, they will continue to use it;
- **How will the role of FDA change?** FDA is not legally charged with the responsibility of making drugs affordable. But it doesn't mean such question doesn't exist. Drug affordability is an issue in the US political landscape. It will get addressed regardless of who;

To change FDA's decision priority from protecting innovation to considering cost benefit will take time. But we believe it will eventually happen.

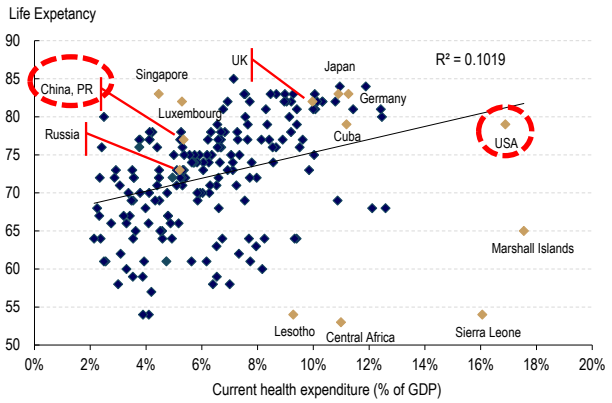
The recent FDA deliberations on Chinese PD-1/L1 offer a glimpse of what might be ahead. FDA does not consider cost or drug pricing in its regulatory decision making. Instead, private and public insurers, physicians and pharmacist have the responsibility for cost-benefit decision making. However, such statement is a dilemma. Without FDA approval, insurers, physicians and pharmacists have a narrow selection of choices to exercise their responsibility. It thus eventually boils down to a coordinated industry policy of paying how much to encourage and protect innovation before the arrival of Chinese innovative drugs become an more obvious issue.

Exhibit 34. US spend more than average on healthcare



Source: WHO, BLRI (2021/10/21). Current healthcare exp. excl. investments

Exhibit 35. Yet it does not reflect on life expectancy



Source: WHO, BLRI (2021/10/21). Current healthcare exp. excl. investments

As Exhibit 34 and 36 show, the percentage of healthcare expenditure of GDP of US (17%) is substantially higher than world average (10%) and China (5.4%), yet the life expectancy of US is below the global trend line when most developed countries and China are above. There are various explanations for this but the appeal for reform is strong and will likely get stronger in the US.

In the meantime, Chinese innovative drug developers are sandwiched between two opposing forces:

- **The pricing pressure from China's state healthcare complex on innovative drug is going to stay**. China is drastically underfunded in social security. As Exhibit 36 shows, the average pension asset distributed over popular over 65 was only US$10K in 2021, comparing to US$722K for US and US$107K for Japan and US$105K for South Korea. Such underfunding is due to the short history of China's state pension and health insurance scheme, as well as China's lack of investment vehicles for these two funds;

US healthcare is expensive, but US pensioners have the assets to pay for it, for now. While the same is not true for Chinese elders.

- **The US pensioners have enough balance in their retirement account to pay for high drug prices, for now:** The high pension assets held by US retirees offset the weak balance sheet of the US public health insurance programs, as shown in Exhibit 37, rendering the need for reform less urgent;

Exhibit 36. China's pension asset vs. the world, 2021

(US$ tn)	China	US	Japan	Korea	India
National	1.38	2.85	1.97	0.56	0.07
Employer	0.65	23	1.10	0.19	0.01
Individual	0.02	14	0.75	0.14	0.004
Total	2.05	39	3.82	0.89	0.09
Population >65 (mn)	201	54	36	8.5	91
Pension per senior (US$ K)	10	722	107	105	1.0

Source: MOHRSS, SSA, BOJ, GPIF, PFA, NPFA, KOSIS, NPS, Blue Lotus (2022/10/21). Exchange rate assumptions, US$1=Rmb6.8=JPY137=KRW1,333= INR80

Exhibit 37. Public health insurance comparison, 2021

(US$ bn)	China	USA	Japan	Korea	India
Premium	422	888	92	56	0.41
Payment	(354)	(839)	(90)	(55)	(0.21)
Profit	69	48	2.0	1.12	0.20
Balance	532	326	60	16	NA
Population (bn)	1.43	0.34	0.12	0.05	1.42
Balance per capita	373	964	486	300	NA

Source: NHSA, CMS, MOHFW, E-STAT, KOSIS, Blue Lotus (2022/10/21). Exchange rate assumptions, US$1=Rmb6.8=JPY137=KRW1,333= INR80

Developing drugs in China is cheap, but is getting expensive

Why is developing drugs so cheap in China? Will it continue? The answers to this question might have several angles:

- **At least some Chinese innovative drugs may not be as cheap if litigation cost is included:** At the present time, there has been no material litigation outstanding, in public, against the Chinese innovative drug developers. But this might be due to: (1) minuscule sales impact outside of China, (2) fear of retaliation, (3) faster follower strategy adopted by Chinese innovative drug developers means patent infringement possibility might have been already planned at the time of development. However,

We expect CDE (NMPA) to slow down approval but the long-term trend of fast approval will not change, in our view.

  - **Accusations about molecular similarity have been levelled against Chinese drug developers in the past**. Besides CSPC, HENGRUI was also accused of infringement in the past;
  - **Patent litigation is commonplace when large enough revenues are involved**. In January 2017, Ono Pharmaceutical and its licensee BMS settled their lawsuits against Merck on *Keytruda*, in which Merck must pay BMS and Ono US$625mn royalties, plus 6.5% of *Keytruda* revenues from 2017 to 2023 and 2.5% from 2024 to 2026. BMS, which acquired Ono's co-developer Medarex in 2005, laid claim on the Ono patents which also won cases against Roche on *Tecentriq* in 2020 and is now litigating against AstraZeneca on *Imfinzi*. The Ono patents

expire 2023-25. This is a good case of patent litigation happening when drug revenue gets big;

- **Global pharms have extensive patents in key technology platforms**: BMS has extensive patents on CAR-T after acquiring Juno/Celgene in 2018/19. Daiichi Sankyo (4658 JP, NR) in August 2022 won a patent infringement case against Seagen (SGEN US, NR), from which RemeGen (9995 HK, BUY, HK$102) licensed its ADC (Antibody Drug Conjugates) technology and to which also licensed its ADC product. It is therefore possible Daiichi Sankyo might lay patent claim on ADC-related products by RemeGen, too.

Simple clinical trial design can save up to ~80% of trial cost.

- **Fast and loose approval by CDE (NMPA) cuts costs**: CDE approved 15 PD-1/L1 (11 domestic, 4 imported) from 2018 to 2022 while FDA has approved only 7 since 2014. Most Chinese PD-1/L1 received conditional approval from NMPA with single-arm test (no placebo but comparing against third party or historical data). A study conducted on 39 Phase III oncology clinical trials in the US (*Source: Emily Han-Chung Hsiu, et.al, Clinical Trials*, *April 2020*) between 2015-17 showed double-arm (with placebo) cost 3.2x of single-arm and measuring Overall Survival Rate (OS) cost 87% more than measuring Progression Free Survival (PFS), which in turn cost 139% more than measuring Overall Response Rate (ORR). More Chinese innovative drug developers than their US peers used single-arm and ORR to conduct their clinical trials;

Overcrowding is another reason why Chinese carcer drugs are so cheap.

- **Chinese innovative drug developers adopted a fast follower strategy to concentrate scientific manpower and low CXO and clinical costs**: Various studies have put the cost of China's clinical trial cost to be 1/6 to 1/2 of that in US. Such comparisons must be made under the same trial design so it warrants a grain of salt. Exhibit 38 presents an imperfect comparison of US data from a recent study published in 2020 and Chinese data drawing from listco disclosures. It seems clinical trials conducted in China is indeed cheaper than US in most cases. Further, Chinese innovative drug developers heavily bet on oncology from the start, conducting 2/3 of their pivotal clinical trials (Phase III and IV) in 2017. This ratio climbed and peaked in 2018 at 78%. US, on the other hand, typically conducts only 25-40% of its clinical trials on oncology (Exhibit 39). The number of oncology clinical trials conducted in China overtook US in 2019. Over-crowding and scale economy might both contribute to low drug price;

Clinical trials in China are 1/6 to 1/2 of the cost in US.

- **Production of drugs in cheaper in China**: China is the largest producer of Active Pharmaceutical Ingredients (API) with ~40% global market share (*Source: Optima Insights*). This also contributed to the rise of CDMO (Contract Development and Manufacturing Organization) in China, including our CXO top pick Wuxi Biologics (2269 HK, BUY, HK$88). Proximity of innovative drug developers with CRO/CDMO's, together with China's dominance in API, contributes to lower cost of production in China;

Many Chinese universities have the set up of life science colleges to produce educated labor in life science.

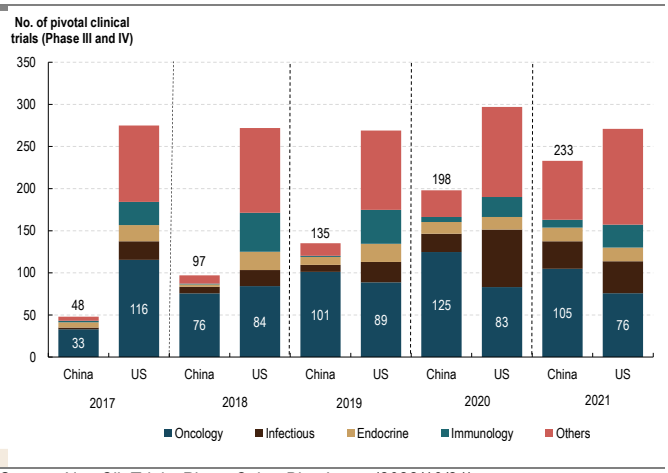
- **China produces large quantity of educated labours in life science**: Life science started receiving government support many years ago. Many Chinese universities have the setup of life science colleges while such has never taken place in the US. Such education had produced many PhD students studying in US universities.

Exhibit 38. Est'd pivotal clinical trial cost in US & China

K US$ per patient	US	China
Blood	311	53
Oncology	100	42
Musculoskeletal	58	NA
Respiratory	54	34
Endocrine	41	NA
Genitourinary	40	NA
Central nervous system	39	NA
Infectious	37	NA
Cardiovascular	35	18
Gastrointestinal	28	NA
Dermatology	25	NA
Ophthalmological	24	31
Overall	41	NA

Source: Moore TJ, et al. *BMJ Open*, Disclosure by Sino Celltech (688520 CH), Bio-Thera (688177 CH), CNKH (002773 CH), Staidson (300204 CH), Salubris (002294 CH), Blue Lotus (2020/10/21)

Exhibit 39. Number of pivotal clinical trials, China vs. US



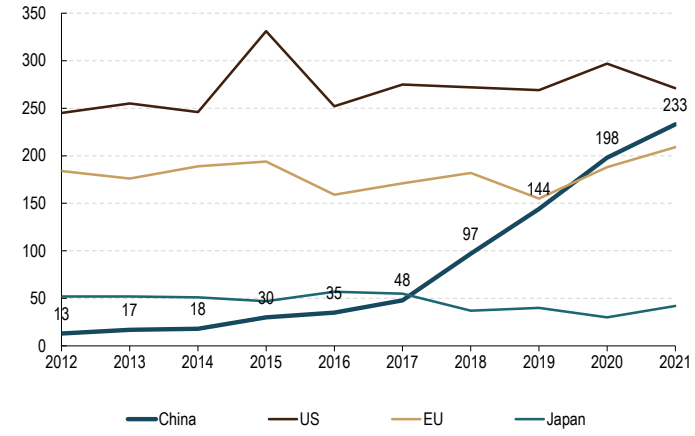
Source: NextClinTrials, PharmCube, Blue Lotus (2022/10/21)

China is catching up rapidly in research quality and quantity

As Exhibit 40 shows, the number of pivotal trials (Phase III and IV) conducted in China rapidly climbed from 25% of Japan, 7% of EU and 5% of US in 2012 to 5.5x of Japan, 1.1x of EU and 86% of US. The major driving force for this was oncology but other therapeutic areas also saw sustained growth in recent years.

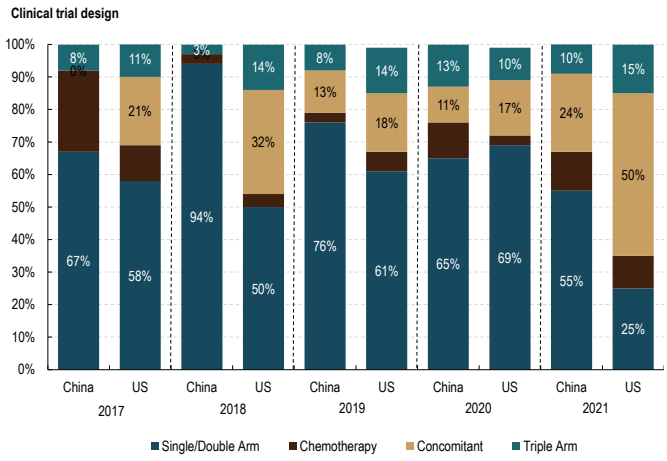
Quantity, quality and composition of pivotal clinical trials have seen rapid growth in China in recent years.

Exhibit 40. Number of pivotal clinical trials comparison



Source: NextClinTrials, Blue Lotus (2020/20/21)

Exhibit 41. PD-1/L1 clinical trial designs, China vs. US



Source: NextClinTrials, Blue Lotus (2020/20/21)

The quality of these trials also improved as shown in PD-1/L1's trial designs (Exhibit 41). Low quality single/double arm (no placebo or dummy placebo) trials peaked in 2018 at 94% in China and has since come down to 55% in 2021, vs. 25% in the US, which also came down markedly, thanks to tightening approval from the FDA. In the meantime, high quality triple-arm (active control placebo) rose from 8% in 2017 to 10% in 2021, comparing to 15% of US. As PD-1/L1 trials exploring concomitant drug usage (multiple drugs in one trial), Chinese innovative drug makers also quickly followed from 2019 onwards, contributing 24% of total in 2021, comparing to 50% of the US.

The paces of industry evolution and regulatory decision have shown a lot of synchronization between US and China.

See the last page of the report for important disclosures

Race to biopharma completed qualifying round

Things are turning to the better.

Sandwiched between a price sensitive Chinese health authority and a price insensitive US regulator, Chinese innovative drug developers must navigate to a future point when China becomes less price sensitive while US becomes more price sensitive. We believe this is a possible goal, but the transitional period can last one to two decades. Out of the 61 biotech's listed on HKSE and STAR SSE, the majority will go under, in our view, yet it doesn't conflict with the scenario that in 10-20 years there will be a universe of ~200 biotech's with several dozens of investible ones. We believe not all biotech's should transformation into biopharmas. The preparation and timing are both important. Out top pick is BeiGene (BGNE). Our long-term pick is RemeGen. Our new-comer pick is Akeso.

Not all biotech's will graduate into biopharmas

Biotech sells IP (R&D only) while biopharma sells product (R&D+Sales). The divergence is taking place now. But this transformation is not a one-way street.

Traditional pharmaceutical companies (pharma's) focus on chemical processes and small molecules while biotech companies focus on biological processes and big molecules. Biotech sells intellectual properties (IP) while biopharma's sell products. Developing a drug bears some resemblance to developing a game but the difference is disease population and existing therapies are usually known while popular taste for game is usually unknown. Just like many game developers staying as developers, there is nothing wrong, in our view, with biotech's staying as biotech's.

Pharma/Biopharma are the orchestrator of the innovative drug value chain

After the recent PD-1/L1 and IPO boom, many Chinese innovative drug makers are now on the verge of separating from biotech's to biopharma's. Based on our observation, the space can be divided into three camps:

- **Traditional players, including:**
    - **Generic drug maker turned biopharmas,** such as HENGRUI (600276 CH, NR), SinoBio (1177 HK, NR), CSPC (1093 HK, NR) and QILU Pharma (private);
    - **Supply chain (sales) turned biopharmas**, such as FOSUN Pharma (2196 HK, NR), HUTCHMED (HCM US, NR), China Medical Systems (867 HK, NR), Zai Lab (ZLAB US, HOLD, US$30) and Henlius (2696 HK, NR);
    - **Supply chain (CRO/CDMO) turned biopharmas**, such as GenScript (1548 HK, NR) and JW Therapeutics (2126 HK, NR)
- **Biotech-turned-biopharmas** includes BGNE, RemeGen, Innovent, JUNSHI, Akeso and LEGN;
- **Biotech's** are plenty, including Alphamab (9966 HK, NR), Ascentage (6855 HK, NR), Biocytogen (2315 HK, NR), CARsgen (2171 HK, NR), Cstone (2616 HK, NR), Everest (1952 HK, NR), InnoCare (9969 HK, NR), I-Mab (IMAB US, NR), KelunBio (2422 CH, NR), KeyMed (2162 HK, NR), LEPU (2157 HK, NR), etc.. There are also vaccine biotech's CanSino (6185 HK, NR), RecBio (2179 HK, NR) and Walvax (300142 CH, NR).

The reason many supply chain and generic drug makers getting into innovative drug development is because of the global boom of medical discovery in big molecule, immunotherapy and genetics.

The reason so many value chain players getting into innovative drug development is because of the global boom of medical discovery in big molecule, immunotherapy and genetics, which result in many development opportunities of discontinuity.

The roles of pharma and biopharma are desirable because they occupy the central role of orchestrator in the value chain of innovative drug industry. We believe this set up is going to continue because drug discovery is decentralized and unscalable, while regulatory approval and drug marketing to finite number of regulators, hospitals and doctors are centralized and scalable. An investible business requires the combination of growth and scalability to be investible. To this end it is understandable that biotech's wants to transform themselves into biopharmas. But an ill-prepared or wrong-timed one can turn into disaster.

Generic drug maker turned biopharma has stable revenue and profit, but their revenue is sales driven. NDRL exerts constant pricing pressure on their legacy products.

Traditional pharma's leverage sales force and regulatory

HENGRUI and **SinoBio** originate from generic drug and thus maintain large sales forces and product revenues. They are also familiar with the regulatory apparatus. In C1H21, HENGRUI disclosed its revenue split between innovative and generic drug to be 4:6. In C1H22, SinoBio disclosed its revenue contribution from innovative drug to be 23%. We note that HENGRUI and SinoBio, together with their traditional pharma peers CSPC (1093 HK, NR), Livzon Pharma (1513 HK, NR) and QILU Pharma (private), produce chemical drugs that are subject to increasing pricing pressure from state collective procurement.

HENGRUI has superior sales ability to drive Camrelizumab to No.1 selling PD-1/L1 in China, but the drug's out-licensing road is bumpy due to its side-effects.

We notice that HENGRUI's sales force of 13-17K was 50-60% of its total employee base. This ratio appears high relatively comparing to sales-oriented global pharma's like Novartis and GSK and absolutely comparing to research-driven global pharma's like Merck (Exhibit 42 and 43). On the other hand, RemeGen has low percentage of sales in its employee base.

Exhibit 42. Product revenue and sales force size

	2019	2020	2021
Product revenue as total			
HENGRUI	100%	100%	100%
SinoBio	98%	98%	98%
BeiGene (BGNE)	52%	100%	54%
Innovent	97%	62%	94%
JUNSHI	100%	69%	11%
RemeGen	NA	NA	9.1%
Zai Lab	100%	100%	100%
Legend	0%	0%	0%
Sales marketing employee as total			
HENGRUI	60%	59%	54%
SinoBio	NA	NA	51%
BeiGene (BGNE)	26%	NA	43%
Innovent	35%	41%	50%
JUNSHI	NA	37%	30%
RemeGen	NA	7.1%	15%
Zai Lab	43%	50%	48%
Legend (LEGN)	NA	2.7%	5.6%
Merck	24%	24%	21%
GSK	39%	39%	39%
Novartis	41%	40%	40%

Exhibit 43. Revenue and total employee

	2019	2020	2021
Revenue (US$ mn)			
HENGRUI	3,367	4,110	4,013
SinoBio	3,504	3,504	4,161
BeiGene (BGNE)	428	309	1,176
Innovent	152	570	662
JUNSHI	112	236	624
RemeGen	-	-	222
Zai Lab	13	49	144
Legend	57	76	90
Total employee			
HENGRUI	24,431	28,903	24,491
SinoBio	NA	NA	25,579
BeiGene (BGNE)	3,400	5,100	8,000
Innovent	1,982	3,200	5,568
JUNSHI	1,421	2,453	2,805
RemeGen	NA	1,366	2,121
Zai Lab	692	1,194	1,951
Legend (LEGN)	NA	882	1,071
Merck	57,036	58,096	68,000
GSK	99,437	94,066	90,096
Novartis	103,914	105,794	104,323

See the last page of the report for important disclosures

Source: HENGRUI, SinoBio, BEIGENE, Innovent, JUNSHI, Zai Lab, Legend, Blue Lotus (2022/10/21)

Source: HENGRUI, SinoBio, BEIGENE, Innovent, JUNSHI, Zai Lab, Legend, Blue Lotus (2022/10/21)

The challenge faced by traditional pharma's in their transitioning to innovative drug developer are two folds. One, their sales aren't used to sell innovative drugs. Later, after inclusion to NDRL, less sales effort is needed to sell the included drugs. Early movers like HENGRUI and SinoBio successfully retrained their sales force but still need to cut headcount aggressively post NDRL. Secondly, these drug developers aren't familiar with regulatory and marketing outside of China. As overseas revenue becomes increasingly important, they are ill prepared.

SinoBio has been successful in incubating outside of the company.

Camrelizumab's (HENGRUI) claimed sales leadership among domestic PD-1/L1 market but its out-licensing record is zero. It was licensed to Incyte in 2015 but returned in 2018, following discovery of side effects.

Lately, HENGRUI and SinoBio started to incubate outside the company. In May 2022, HENGRUI formed a subsidiary called Luzsana in Basel, Switzerland to coordinate its pipeline sales overseas, with the ex-CCO of Merck Europe as its CEO. We observe all clinical trials overseas are now conducted under the corporate brand of Luzsana.

In June 2022, SinoBio, though its London subsidiary Invox, announced plan to acquire F-Star (FSTX US, NR) for US$161mn. F-Star has a BsAb focus. The deal is now under CFIUS (Committee of Foreign Investment in US) review.

SinoBio established Invox in March 2021 and has since then acquired several European biotech startups. In 2019, SinoBio led the Series D investment in Akeso. It further secured the sales right for Akeso's first PD-1 mAb Penpulimab in China. In 2015, SinoBio subscribed to a convertible bond offering of a life science venture capital firm Karolinska Development in Sweden (KDEV SW, NR) and subsequently increased its stake to 48% in February 2022 (*Source: Companies*).

Supply chain turned companies leverage sales and manufacturing

One third of FOSUN's profit came from its 51:49 JV with stated owned China National Pharmaceutical Group Corporation (CNPGC) in drug wholesaling.

FOSUN Pharma (2196 HK, NR), **China Medical Systems** (CMS) and **GenScript** pharmaceutical supply chain companies focusing on sales, channel or outsourced manufacturing. Their entries to innovative drug development leverage their distribution and manufacturing prowess.

In 2021, FOSUN Pharma had a drug commercialization team of 6,000+, including 1,000+ focusing on overseas (*Source: FOSUN Pharma Annual Report*). This is bigger than many biopharma's. It owns 49% of Sinopharm's (1099 HK, NR) parent company Sinopharm Industrial. The other shareholder is China National Pharmaceutical Group Corporation (CNPGC), the state drug monopoly. Sinopharm is China's largest drug wholesaler. About 3/4 of FOSUN's 2021 revenue of Rmb39bn was from manufacturing of generic or licensed drugs, including BioNTech's COVID vaccine. But ~1/3 of its Rmb2bn of net profit was through earnings recognized by equity-method from Sinopharm through drug wholesaling. Similarly, CMS was founded as a drug sales force and GenScript started and still has business as a contract manufacturer (CDMO).

All three have ventured into biotech through subsidiaries. FOSUN Pharma formed innovative drug and biosimilar subsidiary **Henlius** (2696 HK, NR) and cell therapy (CAR-T) JV with Kite, a subsidiary of Gilead Science (GILD US, NR). GenScript incubated **Legend Biotech** (LEGN US, SELL, US$16), which is 57% owned by GenScript. Another CAR-T biotech, **JW Therapeutics** (2126 HK, NR), is the JV between WuXi AppTec (2359 HK/603259 CH, NR) and Juno, a subsidiary of BMS.

Wuxi AppTec gets into CAR-T through a JV with Juno.

The challenge faced by supply-chain-turned biopharma is their abilities to get truly FIC drugs at a reasonable price, on time. FOSUN's subsidiary Henlius (2696 HK, NR) focuses mainly on biosimilars. Among the 5 commercialized products sold by Henlius, 3 are biosimilars, 1 is licensed and only 1 (Serplulimab) is self-developed. However, Henlius managed to license out its biosimilars to 3rd parties, such as Organon (OGN US, NR), Abbott (ABT US, NR), Europharma and Getz, mostly to sell in developing countries. We believe Henlius has successfully carved a niche leveraging FOSUN's global network. Whether it can leverage Serplulimab to turn itself into a biopharma remains to be seen.

Henlius's selling of biosimilars to developing countries leveraged FOSUN's global network, in our view.

FOSUN Kite (复星凯特) and JW Therapeutics (药明巨诺) act as the Chinese distributor of Kite's Axicabtagene Ciloleucel (*Yescarta*), which was approved by NMPA in June 2021 and BMS's Relmacabtagene Autoleucel (*Carteyva*), which was approved by NMPA in September 2021. Both are CAR-T's.

Biotech's stand to produce the most number of biopharmas because they control products.

Biotech turned biopharma's leverage on product

The advantage of biotech is the control of products. BGNE, Innovent, JUNSHI, RemeGen and Akeso are at various stages of transforming into a biopharma. BGNE has already completed this transformation. Innovent and JUNSHI have run into various degree of difficulties. RemeGen has been the most conservative and Akeso is about to start the journey.

As Exhibit 42 shows, **JUNSHI**'s product sales as total revenues have declined for the past two years and its commercialization strategy has flipped from licensing to AstraZeneca China in February 2021 to building in-house in December 2021 and has changed four sales heads. Toripalimab was the first approved PD-1/L1 drug in China in 2018 for Melanoma, a relatively small indication of ~8,000 new patient per year. But for the entire 2019 and 2020 Toripalimab received no additional indication approvals, opening the room for competitors to catch up. Because of this ill executed commercialization, by 2021 Toripalimab has slipped to the 4th place for domestically developed PD-1/L1 China, falling behind Camrelizumab (HENGRUI), Sintilimab (Innovent) and Tislelizumab (BGNE), as shown in Exhibit 32.

JUNSHI has lost hard-earned first-to-market advantage in PD-1/L1 due to slow indication approval and wavering sales strategy.

Innovent has an aggressive buildup strategy. Its FDA approval for Sintilimab was rejected. Yet Innovent is still building out its sales force, reaching 2,768 by the end of 2021 and further to >3,000 by C1H22, according to disclosure. By C1H22 Innovent's salesforce has covered >5,000 hospitals out of a total of 36.6K, of which only 1,651 were Class-III-Grade-A hospitals (三甲) likely capable of treating cancer patients.

Innovent is pushing ahead of commercialization buildup despite setbacks of fierce PD-1/L1 competition, FDA rejection and lack of late stage products.

Innovent does have a comprehensive pipeline spanning Oncology (25 drug candidates), Autoimmune (4), Metabolic (2) and Ophthalmology (3). However, the closest towards commercialization is a

Metabolic drug treating generic-caused high cholesterol levels (IBI306). According to literature (*Source: "Current Status of Familial Hypercholesterolemia in China"*, *Peipei Chen, et.al*, Front Physiol., 2019), there are 2.8-6.9mn Heterozygous Familial Hypercholesterolemia patients (HeFH) in China, which are IBI306's target. However, treatment of HeFH with Statin-typed drugs has generally been effective and high cholesterol level isn't life threatening. We estimate IBI306 will likely be a hundred-million-dollar-a-year class of drug.

BeiGene (BGNE) stands the best chance to become a global biopharma

BGNE today has two strong selling drugs to support its transition into a biopharma. In 2021, self-developed Zanubrutinib (*BRUNKINSA*) contributed US$218mn of revenues, up from US$42mn in the prior year. It now has regulatory approval in 50 countries. We estimate Zanubrutinib's China-vs-international revenue split to be 46:54 in 2021.

BGNE has the most diversified product portfolio and sales footprint.

Self-developed PD-1/L1 Tislelizumab's China sales reached US$255mn in 2021, becoming the 3rd top selling PD-1/L1 in China (Exhibit 32). Its US approval is still pending. In C1H22, China sales of Tislelizumab reached US$193mn, surpassing Sintilimab's (Innovent) US$159mn (*Source: Eli Lilly*) and Toripalimab's (JUNSHI) US$45mn (*Source: JUNSHI*) to rank No.2 behind HENGRUI's Camrelizumab.

BGNE has a diversified revenue stream. Revenues from China contributed 52%, 94% and 44% of revenues in 2019-2021. BGNE licensed ex-China rights of Tislelizumab and Ociperlimab to Novartis. It also sells Zanubrutinib (*BRUKINSA*) by itself in developed countries and licensing it out in developing countries (Adium for Latin America and the Caribbean, NewBridge for Middle East and North Africa, Erkim for Turkey, Nanolek for Russia, and Medison for Israel).

BeiGene's Zanubrutinib (BRUKINSA) has won head-to-head clinical trial against the 7th largest drug in the world in 2021.

We are particularly positive on Zanubrutinib because of its superior head-to-head trial result against main competitor Ibrutinib (*Imbruvica*) of AbbVie/J&J's, which is known to cause cardiovascular adverse effects. Yet AbbVie and Johnson nevertheless successfully grew Ibrutinib to become the 7th top selling drug in the world, grossing US$9.8bn in 2021 (*Source: AbbVie & Johnson & Johnson*). Both BGNE's Zanubrutinib's (*BRUKINSA*) and AstraZeneca's Acalabrutinib (*Calquence*) won head-to-head clinical trials against Ibrutinib but Zanubrutinib, in particular, has won by superior efficacy as well as better safety. Hence, we are more positive on Zanubrutinib.

Sotorasib (LUMYKRAS) is showing promising result in BGNE's late-stage pipeline. So is Adagrasib, a similar drug in ZLAB's late-stage pipeline.

Such head-to-head clinical trial hasn't been conducted on Tislelizumab and we doubt it will produce as positive a result. Therefore, we believe Tislelizumab will likely derive more revenues in China than out of China even after its FDA approval. Considering Ibrutinib sold US$9.8bn and Acalabrutinib (AZ) sold US$1.2bn a year, Zanubrutinib's global sales should exceed US$2bn by its peak year, a ten-fold increase from 2021.

In terms of late-stage pipeline, BGNE has Ociperlimab (BGB-A1217), a TIGIT inhibitor oncology drug that is in Phase III. It also collaborates with Amgen for the launch of Sotorasib (*LUMYKRAS*), a KARS inhibitor treating non-small cell lung cancer (NSCLC), in China. Sotorasib won FDA fast track (conditional) approval in May 2021. In September 2022, Amgen presented positive clinical result for Sotorasib for the treatment of NSCLC in ESMO (European Society for Medical Oncology) Annual Congress, substantiating FDA's approval decision. Sotorasib faces competition from Adagrasib, a similar drug in ZLAB's pipeline.

ZLAB's short term pipeline launches contain several treasures

Zai Lab's (ZLAB US, HOLD, US$30) go-to-market strategy is to be the go-to-person for the dispersed global biotech industry to access the China market, the world's 2nd largest by country.

Bringing cutting edge drug around the world to the world's 2nd largest pharmaceutical market, China, is a viable business.

ZLAB currently has 9 license-in products in pivotal clinical stage with 15 indications sought, 2 of which have already received FDA approval. All four selling drugs/therapies of ZLAB have received FDA approval (Exhibit 48).

Within ZLAB's late-stage pipeline there are two drugs we think can produce sizable revenues:

BGNE and ZLAB's pipeline overlaps in two drugs: Pamiparib/Niraparib and Sotorasib/Adagrasib.

- **Repotrectinib** (瑞波替尼) is a broad-spectrum multi-targeting Tyrosine Kinase Inhibitor (TKI) developed by Turnpoint Therapeutics (TPTX US, NR) which was acquired by BMS for this drug on June 8, 2002 for US$4.1bn. ZLAB signed for Greater China distribution in July 2020;
- **Adagrasib** (阿达格拉西布) competes against Amgen/BGNE's Sotorasib for treating advanced KRAS G12C-mutated cancer. ZLAB signed for Greater China distribution of Adagrasib with Mirati Therapeutics (MRTX US, NR) in July 2021.

Despite Innovent's aggressive buildout of sales team, it remains a one drug company with a number of license-ins and biosimilar drugs.

ZLAB also pioneered the category of PARP Inhibitor in China with its flagship drug Nariparib (*ZEJULA*). However, with the recent recall of three PARP Inhibitors in US, including ZEJULA, all PARP inhibitors are now at risk. This includes BGNE's Pamiparib, a Phase III candidate already selling in China on a conditional approval basis and Senaparib (JS109) of JUNSHI.

Both Innovent and JUNSHI have gaps in their late-stage pipelines

As shown in Exhibit 48, out of Innovent's 7 drugs in its late-stage pipeline, 5 are licensed-in and 1 is a biosimilar. Further, among Innovent's 7 currently selling drugs, 4 are biosimilars and 2 are licensed-in's. Only one (Sintilimab) is in-house developed. Innovent remains a one-drug company.

JUNSHI has two in-house drugs in pivotal stage but both face crowded competitions.

JUNSHI is in a better situation. It also has only 1 in-house selling drug. But it has 3 in-house drugs in the pipeline entering pivotal clinical stage:

- **JS002 (Ongericimab)** is a PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) treating high cholesterol (Hyperlipidemia), competing against Innovent's IBI306, Akeso's AK102 (Ebronucimab) and HENGRUI's SHR-1209 to try to take market share from Statin-type existing drugs like Pfizer's Atorvastatin (*Liptor*) and several others like Crestor (generic), Ezetimibe (Merck), *Praluent* (Sanofi), *Repatha* (Amgen), Leqvio (Novartis), etc. Competition is severe but indication isn't life threatening, capping the upside of revenue, in our view;
- **JS109 (Senaparib)**, a PARP inhibitor, is co-developed with Impact Therapeutics, competing against ZLAB's Niraparib (*ZEJULA*) as well as HENGRUI's Fluzoparib and AstraZeneca's Olaparib (*Lynparza*) for the narrow indication of Ovarian Cancer;
- **JS016 (Etesevimab)** which is an in-house developed oral COVID drug licensed out of China to Eli Lilly and **VV116 (JT001)**, another oral COVID drug. JUNSHI recognized US$245mn royalty income from Eli Lilly in 2021. JUNSHI has worldwide license right for VV116 but as the global pandemic entering closing stage, the prospects for oral COVID drug are diminishing, especially when Pfizer's *Paxlovid* is aggressively cutting prices worldwide.

In the meantime, JUNSHI also develops biosimilars, such as UBP1211, which is a biosimilar to Adalimumab (*Humira*), the No.2 top selling drug worldwide by AbbVie. Innovent also sells an Adalimumab biosimilar by the trade name of *SULINNO*.

JUNSHI has leadership in oral COVID medicine but may not be able to monetize it as global pandemic drawing to an end.

RemeGen sets itself apart from a different angle and is now leading in ADC

While PD-1/L1 is one type of drug, ADC (Antibody Drug Conjugate) is one category of drugs. An ADC drug uses a linker to link a big molecule biotarget (antibody) with a small molecule toxin (payload). The antibody binds to the cancer cell and the payload kills it.

ADC is a proven drug making platform.

ADC's business advantage is its high technical barrier and is by design a differentiated drug through the choice of antibody, payload drug and linkage. The combination of the three has made the discovery process very complex. In particular, to link an antibody which is big molecule and the payload which is a small molecule and maintain stability in the microenvironment around the carcer is a daunting task. As a result, only a handful of companies have proven technology platforms and their extensibility is questionable.

As Exhibit 44 shows, 6 out of the top 10 ADC drugs likely have intellectual properties (IP), mostly linkers, from Seagen. RemeGen also licensed IP from Seagen but it also licensed Disitamab Vedotin (*Aidixi*) back to Seagen for a huge sum.

RemeGen tailored indication for Aidixi to differentiate against Kadcyla, Adcetris and soon Enhertu.

In August 2022, an arbitration court ruled that Daiichi Sankyo's Trastruzumab Deruxtecan (*Enhertu*) did not violate Seagen's linker patents, reversing two rounds of earlier court rulings. While this ruling was neither final nor did it nullify Seagen's IP claim against other parties, it does enhance *Enhertu*'s marketability, which is already showing potential to be a top ranked drug. *Enhertu* filed for NMPA approval in March 2022 and again in August 2022, both for breast cancers through its ex-Japan distributor AstraZeneca. Before that, Roche's Trastuzumab Emtansine (*Kadcyla*) was approved for breast and gastric cancers in 2020 and 2021 and Takeda's Brentuximab Vedotin (*Adcetris*) was approved for Lymphoma and Squamous Cell Carcinoma in 2020 and 2022 by NMPA. Both drugs are old. Given *Enhertu*'s wide indication record in breast, gastric, lung and colon cancers, it will likely soon surpass *Kadcyla* and *Adcetris* to become the top selling ADC drug worldwide. Approval in China is likely in C4Q22 to C1Q23, in our view.

RemeGen's Disitamab Vedotin (*Aidixi*), or RC48, was approved in China in June 2021 and January 2022, first for Advanced or Metastatic Gastric Cancer and then for Urothelial Carcinoma. In our view, RemeGen chose indications carefully so it will not compete head-to-head against *Enhertu* or even *Adcetris,* on breast cancer. In December 2021, *Aidixi* (RC 48) entered NDRL and its price dropped 72% but was still only 10% cheaper than *Kadcyla* as Roche has actively participated in multiple rounds of NDRL negotiations as well. Launched in 2013 but approved in China in 2020, *Kadcyla*'s price started low and has dropped 56% after it entered NDRL. Everest Medicine licensed Sacituzumab Govitecan (*Trodelvy*) from Gilead to China but returned the right back on August 2022. *Aidixi* (RC 48) costs 10% to 25% of comparable drugs in the US.

Aidixi (RC 48) is 10% cheaper than Kadcyla, a drug that is almost 10 years on the market. It is 10-25% of comparable drugs in the US.

Our forecast is for *Enhertu* to start in China with a high price to be in-line with its global pricing. But a price war cannot be ruled out after *Erhertu* receives more indications from NMPA, likely in the 2024-25 time-frame.

Exhibit 44. Top 10 ADC drugs worldwide

Exhibit 45. ADC drug price in China and US

Trade	Made by	IP	First to market	Revenue (US$mn), 2021
Kadcyla	Roche	ImmunoGen	2013	2,178
Adcetris	Takeda	Seagen	2011	1,306
Enhertu	AZ/ Daiichi Sankyo	Daiichi Sankyo	2019	501
Trodelvy	Gilead	Gilead	2020	380
Padcev	Astelles	Seagen	2019	340
Polivy	Roche	Seagen	2019	271
Besponsa	Pfizer	Seagen	2017	192
Blenrep	GSK	Seagen	2020	122
Zynlonta	ADC Therapeutics	ADCT	2021	34
Aidixi	RemeGen	Seagen	2021	13

Source: Biopharma PEG, Blue Lotus (2022/10/21) * Through acquisition of Immunomedics in 2020

(US$)	Trade	Maker	Price/yr. before NDRL	Price/yr. after NDRL	Price in USA
Trastuzumab Emtansine	*Kadcyla*	Roche	96,821	41,878	117,602
Brentuximab Vedotin	*Adcetris*	Takeda/ Seagen	113,759	113,759	390,040
Disitamab Vedotin	*Aidixi*	RemeGen	133,969	37,710	NA
Trastruzumab Deruxtecan	*Enhertu**	AZ/Daiichi Sankyo	NA	NA	161,829
Sacituzumab Govitecan	*Trodelvy***	Gilead	NA	NA	32,0960

Source: Roche, Takeda, Remegen, AstraZeneca, Daiichi Sankyo, Blue Lotus (2022/10/21) US$1=Rmb6.55. * Submitted but not approved. **Approved but not priced.

Up till now, NMPA has approved 4 ADC drugs (Exhibit 45), among which only 1 is domestically developed (RemeGen's RC48), while FDA has approved 12. This shows the barriers of making ADC drugs are higher. **RemeGen** currently has 6 ADC drugs in various stage of Phase I and II clinical.

NMPA only approved one domestically developed ADC so far while FDA approved 12, reversing the patten we saw in PD-1/L1.

Because ADC is a drug development technology rather than a drug, it technically should be an ideal platform for CRO's and in particular, CDMO's. In 2021, Wuxi AppTec and Wuxi Biologics formed a 40:60 JV called Wuxi XDC (药明合联). In C1H22, Wuxi Biologics announced it had secured 76 ADC development projects globally, of which 27 has commenced clinical trials.

Other China biotech's focusing on ADC include: (1) **Kelun Botai**, a subsidiary of Kelun Pharmaceuticals (002422 CH, NR) has signed out-licensing deals with Merck in May and July 2022 for 2 drug candidates, totaling US$2.3bn in consideration. One of these 2 drugs (SKB264/MSD2870) has been in Phase III since April 2022 on breast cancer. Merck has a pending acquisition of Seagen; (2) **LEPU Biopharma** (2157 HK, NR), a subsidiary of medical device maker LEPU Medical (300003 CH, NR), has 5 ADC drugs in various stages of clinical. One, MRG002, is in Phase II/III targeting also breast cancer. In 2021 LEPU acquired ADC biotech Shanghai Miracogen, who obtained its ADC technology from Dutch biotech Synaffix; (3) generic-turned **HENGRUI** has 5 ADC drugs in various stages of early clinical, adopting a fast follower strategy; (4) generic-turned ADC pioneer **Bio-Thera** (688177 CH, NR) has 2 ADC drugs in clinical trials after withdrawing 2 in 2021; (5) **Tot Biopharm** (1875 HK, NR), a subsidiary of Taiwan biotech incubator Center Lab (4123 TW, NR), has 1 ADC in Phase III, (6) **Innovent** signed an IP licensing deal with Synaffix in June 2021. In August 2022 Innovent signed a global collaboration partnership for ADC development with Sanofi; (7) **JUNSHI** invested and partnered with Hangzhou DAC Biotech (private), which has 6 ADC drugs under development in various stages of Phase I-II clinical; (8) **BGNE** signed an IP licensing deal with Seagen in 2019. It has 2 license-in ADC drugs from Zymeworks (ZYME US, NR) in clinical trials since 2018. One of the two signed ex-China licensing deal with Jazz Pharmaceuticals (JAZZ US, NR), (9) SinoBio applied for a global ADC patent (WO2022033578) in February 2022.

Generic-turned Bio-Thera withdrew two ADC clinical trials in 2021, highlighting the difficulty in developing ADC drugs.

ADC is widely deployed in pharma/biopharma/biotech pipelines.

Besides ADC, similar drug-design technology includes PROTAC (Proteolysis-Targeting Chimeras), a small molecule composed of two active domains and a linker, capable of removing specific unwanted proteins. BGNE and Kintor Pharma (9939 HK, NR) each has 1 PROTAC under clinical trials.

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The developing market that doesn't exist for innovative drugs

We analyzed China's healthcare system in our health information system initiation, <*China's digital health: too expensive and too early*>, September 15, 2021. Our conclusion was that China's healthcare system has its unique advantages and disadvantages inherited from a Beveridge Model but underwent a sweeping reform since 1985 to evolve from a universal payor to using an insurance fund to pay for medical expenditures. Such reform was a great success from the angle of enrollment, balance of payment and equitable access. It also changed China's pharmaceutical industry. From the beginning, China's healthcare system emphasizes on cost effectiveness over quality of care. China's medical resource and funding balance also do not permit it to pursue quality over cost in a foreseeable future, as shown in Exhibit 36 and 37. As a result, using NDRL to bring down the cost of healthcare is going to be a national policy in a foreseeable future. Chinese doctors are underpaid comparing to their US counterparts. Chinese innovative drug developers will be too.

Chinese doctors are underpaid comparing to their US counterparts. Chinese innovative drug developers will be, too.

Of course, if Chinese innovative drug developers can hone their skills at home, then they can be globally competitive worldwide. This argument is not necessarily true but we believe it might be more true in an environment when a great divide erects between US and China. In the short term, these are the obstacles:

Developed countries have a solution for drug affordability, which is generic drugs, now contributing 90% of all prescriptions in the US but only 11% of revenues.

- **For developed countries cost effectiveness is a secondary concern and is already addressed by the generic/biosimilar mechanism**. FDA/EMA/PMDA emphasizes on non-inferiority over affordability. Further, according to FDA's <*Office of Generic Drugs 2021 Annual Report*>, currently 90% of all prescriptions in the US are filled by generic drugs already. Only because they are cheap do they not shown in revenues. In 2021, generic drug sold only US$83bn in the US (*Source: IMAC*), merely 11% of the US$776bn total drug sales (*Source: IQVIA*). There is nothing wrong some who can afford to pay get slightly better drugs;

China solved the problem of feeding its citizens with enough drugs, through generics. Now it wants generic to be replaced by innovative.

- **Most drug sales take place in developed countries**: According to IQVIA, developed countries were responsible for 74% of all drugs sold worldwide. The so-called **Pharmerging Countries** (China, Brazil, Russia, India and others) were responsible for 25% while the so-called Low-Income-Countries consumed only 1.4% of drug sales, including generic drugs, in 2021. This is certainly vastly unethical but is the reality. According to our calculation, the major developed countries (North America+EU5+ Japan+Korae+Australia) were responsible for 72% of innovative drugs sold and 44% of the generic and biosimilar drugs sold (Exhibit 46). China alone was responsible for 42% of global generic and biosimilar drugs sold. This left quite small market out of developed countries and China, for both innovative and generic/biosimilar drugs;

- **Drug sales in many developing countries are highly disperse with regulatory barriers**: While markets for developing countries technically have great potential for low-cost drugs, conducting clinical trials on local population and building sales forces for the dispersed local markets are both cost prohibitive, more so without a blockbuster drug in sales. For now, most Chinese innovative drug developers have to rely on local distributor to handle regulation and distribution;

Chinese innovative drug developers must win against generics first at home before they can win abroad.

- **Generic and biosimilar drugs are great competitors in developing markets too:** The global generic drug market was US$320bn in 2021 and biosimilar market was US$13bn (*Source: IMAC*). We estimate generic and biosimilar drugs sold outside of developed countries (North

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America+EU5+Japan+Korea+Australia) were US$178bn a year, representing 36% of total drug sales in these countries (*Source: IQVIA, BCG & Blue Lotus*). China's innovative drug must be materially better than generic and biosimilar drugs to win market share. In fact, China itself is a major market of generic and biosimilar drugs. We estimate generic and biosimilar drugs occupied 83% of drug sales in 2021. Chinese innovative drug makers must first win the war against generic and biosimilars at home in order to win abroad.

The rising importance of globalization at a time of divide

As Exhibit 48 shows, BGNE leads Chinese innovative drug developers in terms of percentage of outstanding clinical trials abroad. But BGNE is the exception. According to clinicaltrials.org, 57% of BGNE's 95 outstanding clinical trials are being conducted out of China, exceeding ZLAB's 53% which are mostly in-licensed from abroad anyway. LEGN and RemeGen were 3rd and 4th at smaller totals but in terms of percentages, no Chinese innovative drug developers exceed 10%. We believe this is a huge gap in trying to commercialize pipelines out of China.

Conducting clinical trials at home might be one key reason why Chinese innovative drugs are cheap to develop.

FDA/EMA/PMDA are global influencers and infrastructure shapers

Conducting clinical trials outside of China is critical for commercializing drugs in both developed and developing countries. Many developing countries, as shown in Exhibit 47 below, accept clinical trial results obtained from developed countries but so far not from China. FDA remains the gold standard for health regulators around the world. The cost argument from Chinese innovative drug developers is counter-intuitive and never-heard-of. It will be hard for them to win market share and get paid for it in Pharmerging Countries and Low Income Countries.

Winning Pharmerging Countries might be first stop of globalization as these countries at least tried, persistently, to have their own healthcare system.

Exhibit 46. Global pharmaceutical industry market size

		By industry		By region	
(US$bn)	**Total**	**Innovative**	**Generic & biosimilar**	**Innovative**	**Generic & biosimilar**
US+Canada	43%	47%	27%	85%	15%
EU4+UK	15%	16%	11%	83%	17%
Japan+Korea +Australia	8.3%	9.0%	5.9%	83%	17%
China	**12%**	**2.6%**	**42%**	**17%**	**83%**
Other developed	8.1%				
Brazil+India +Russia+Other Pharmerging	13%	25%	14%	85%	15%
Low income	1.4%				
Total percentage	100%	100%	100%	NM	NM
Total	1,424	1,091	333	1,091	333

Source: IQVIA, BCG, Blue Lotus (2022/10/21)

Exhibit 47. Clinical trial exemption of certain countries

	Exempt from clinical trials	Note
India	Drugs approved in US, UK, EU, Japan and Australia	Phase I and II only. Phase III must be in India
Indonesia	Any as long as satisfactory	FDA and EMA approved drugs 150 days. Others take 300 days
Pakistan	US, UK, EU, Canada, Australia, Japan	NA
Nigeria	Registered in at least two developed countries	NA
Bangladesh	Australia, France, Germany, Switzerland, Japan, UK, USA	Submit Certificate of Pharmaceutical Products of the seven countries for expedite approval
Mexico	US, Canada, Switzerland, EU and Australia	

Source: CDSCO, Badan POM/BPOM, DRA, NFDAC, MOHFW, DOF, Blue Lotus (2022/10/21)

China's joining of ICH is an important first step

Various national and international organizations have taken the initiative of standardizing and expediting the approval process for innovative drugs. Clinical trial is, without doubt, the most time and resource constraining factor in the approval process. In 2015, the World Health Organization (WHO) designated 36 National Regulatory Authorities (NRA) as Stringent Regulatory Authorities (SRA), most of which were European and North American countries (https://www.who.int/initiatives/who-listed-authority-reg-authorities/SRAs). China, as well as Israel, Korea and South Africa weren't on the list. In 2017, China joined The International Council

China's inclusion in the global pharmaceutical industry is still early, as evidenced by the absence in the SRA list, as well as joining ICH with Taiwan under one roof.

for Harmonisation (ICH) as the 8th regulatory member. Now ICH has 20 members and 34 observers, among which regulatory members are 10. Most NRA's are now on IC and we understand WHO is transitioning its drug standardization initiative in SRA to ICH permanently. However, an examination of the history of ICH shows it dates back to 1990, with FDA, EMA and PMDA as three founding regulatory members. China as a relative late comer, despite being a regulatory member, is still junior in status. China's urgency in joining the global pharmaceutical industry can also be seen from ICH's inclusion of Taiwan as one of the 10 regulatory members.

To this end, BGNE is one of a kind among Chinese innovative drug developers to make a serious push, from many years ago, to globalization. We believe other innovative drug makers pin their hope for growth more towards replacing generic/biosimilar drugs at home, which is also a valid market, as shown in Exhibit 46. But in our view, the line between innovative and generic is not always clear. Efficacy, toxicity and cost are what determines the usage at the doctor's end, which is why we believe the argument about high drug cost in US is somewhat a pseudo proposition.

We believe only BGNE seriously pursue a growth strategy of being a global biopharma. Others probably pin their hope on substituting generic/biosimilar drugs at home.
China's argument of deflating global drug price is essentially about deflating drug R&D.

On September 12, 2022, the US Biden Administration launched a National Biotechnology and Biomanufacturing Initiative to make biotechnology competition as a new front in the rivalry with China. We believe the US taskforce will target China's advantages in bio intermediaries and Active Pharmaceutical Ingredients (API's) and exploit China's disadvantages in getting itself recognized globally for pharmaceutical innovations and the smaller size in revenue terms of China's domestic market. China's trump card, in working with global organizations like ICH, regulators in Pharmerging Countries worldwide and US NGO's, is to bring down drug prices on a global scale. Take into consideration of the generics, the cost benefit competition is a comprehensive competition on breadth, depth and cost combined.

Late (pivotal) stage and after: BGNE and ZLAB lead

From our observation, Chinese innovative drug developers are now suffering the "fatigue" following their (1) harvest of first batch of commercialized drugs, (2) IPO's which replenish their cashes and (3) inclusion to NDRL, which typically brings great boost in the first year, only at expense in the following years. For most, before the harvest of their next key drugs in the pipeline, they must try the following strategies, most of which rely on non-R&D functions of the company.

Using licensed-in to fill pipeline will be common in the next few years as the pace of Chinese innovative drug developers slows.

- **Seeking new indications and new combinations of existing products**: As shown in Exhibit 46, all are pursuing wide trials of new indications and combinational therapies. This befits PD-1/L1's pharmacology mechanism and is why many consider PD-1/L1 strategic;
- **In-house drug progression**: (1) BGNE's TIGIT inhibitor Ociperlimab, (2) JUNSHI's PCSK9 inhibitor Ongericimab (JS002), (3) Akeso's PD-1/VEGF BsAb Ivonescimab (AK112) and (4) Innovent's PCSK9 inhibitor Tafolecimab (IBI306) and CLTA-4 biosimilar (IBI310) are five new drugs that will hit the market soon;
- **License-in of new drugs**: License-in is a strategy pursued by all but some more persistently than others and the results also differ. (1) ZLAB, with its 100% licensed-in business model, leads the pack with 9 drugs in pivotal and after trials, among which we are positive on ROS1/TRK/ALK Inhibitor Repotrectinib (TPX0005) with Turning Point and KRAS inhibitor Adagrasib (MRTX849) with Mirati, (2) Innovent has 4 late stage licensed-in's, among which we are positive on none. Its BCMA CAR-T therapy co-developed with IASO Therapeutics needs US sales ability to commercialize but so far has no US partners; (3) BGNE has 3 late

But the result of license-in also differs. ZLAB and BGNE have focused on business development as a corporate function for a long time and thus has harvested stronger license-in pipelines.

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stage licensed-in which is one KRAS inhibitor Sotorasib (*LUMYKRAS*) with Amgen, one BsAb Zanidatamab with Zymeworks and one RTK Inhibitor Sitravatinib with Mirati. We are positive on Sotorasib; (3) JUNSHI has 3 licensed in's but two are co-developed biosimilars: Bevacizumab (JS501) is a biosimilar of Avastin while Adalimumab (UBP1211) is a biosimilar of Humira, both of which are co-developed with local firms. Its third drug, PARP inhibitor Senaparib (IMP4297/JS109), is developed with a local partner Impact Therapeutics but might be impacted by the September recall of three PARP Inhibitors, including ZLAB's *ZEJULA*, in the US market due to adverse effects.

Although next few years are the ebb years of pure play innovative drug developers, we are the most optimistic about their future because their business model is simpler.

There are innovative drug developers that refuse to resort to license-in's to fill their pipelines at time of void. Both RemeGen and Akeso have no license-in's in their pipeline. This typically corresponds to a slower pace in building up sales, which to us is not a deficiency. We have no problem of biotech's staying as biotech's for a longer period of time. We believe a company must stay focus and develop competencies only when the timing is right.

Generic-turned innovative drug developers like HENGRUI and SinoBio have existing generic drug sales to support their sales forces and fund R&D. But the profit margins of their generic drugs are getting thinner and thinner due to NDRL. We estimate the maximum sales force size for selling oncology drug in China is 3,000. Building an oncology sales team of such size with just one drug is a risky undertaking, in our opinion. But in the case that Innovent and JUNSHI persevered in preserving the over-built sales force until the next round of pipeline harvest, it will pose a big threat to HENGRUI and SinoBio, as both will no longer enjoy a channel advantage in the next round of time to market competitions.

Early-stage pipeline: more diversification is likely the next

We see Chinese innovative drug developers having more diversified pipelines than their previous ones.

Overall, we see big firms like BGNE, ZLAB and HENGRUI maintaining balanced pipelines of large and small molecules. Newly minted biopharma's like Innovent and JUNSHI leaned their pipelines towards covering all the latest technological grounds, while biotech's like Akeso, KeyMed, RemeGen and LEGN stay more focused on certain technologies or therapeutic areas.

Having a timed development program can lead to successive rounds of commercialization that smooth out the revenue growth curve. For example, BGNE's TIGIT drug Ociperlimab, has entered Phase III with a licensing deal with Novartis in the bag while JUNSHI, Innovent and Akeso's TIGIT drug are still in early-stages. Larger companies bet more broadly, can reap the success with first mover but can also waste resources on dud projects. It then comes the opportunity of the smaller firms.

Late comers can leapfrog, as RemeGen, LEGN and Akeso have done in the fields of ADC (CDAC), Cell Therapy and BsAb (Bispecific Antibody). Lastly, PD-1/L1 is a technology platform that everyone benefited from, successfully turning a number of biotech's onto the pathway of biopharma's.

Small molecule drugs constitute sizable contribution of pipelines

Biotech's have more progressive but also riskier early-stage pipelines.

We estimate small molecule drugs constitute 1/3 to 1/2 of the pipelines of BGNE, ZLAB, HENGRUI, JUNSHI and Innovent but contribute much smaller for RemeGen, Akeso and KeyMed. In our view, the role model of Innovent is BGNE, of JUNSHI is Innovent.

mAb is still a key part of everyone's pipelines

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Monoclonal antibody (mAb), as represented by PD-1/L1, is still a key component of everyone's pipelines, representing 1/3 (BGNE, ZLAB, JUNSHI, Innovent, HENGRUI, KeyMed) to 3/4 (Akeso) of the early-stage pipelines of Chinese innovative drug developers. But we can see that BGNE is relying heavily on Amgen and Zymeworks for its mAb/BsAb pipeline, suggesting that in the rapid shifting of early-stage R&D competition, nobody is capable of covering all the ground at all time.

As shown in Exhibit 49, breakthroughs in biotechnology result in different waves of drug making techniques. A sustaining biopharma must manage the life cycles of different waves.

As Exhibit 50 shows, ADC, BsAb, PROTAC and CAR-T are fields seeing concentrated bets after mAb.

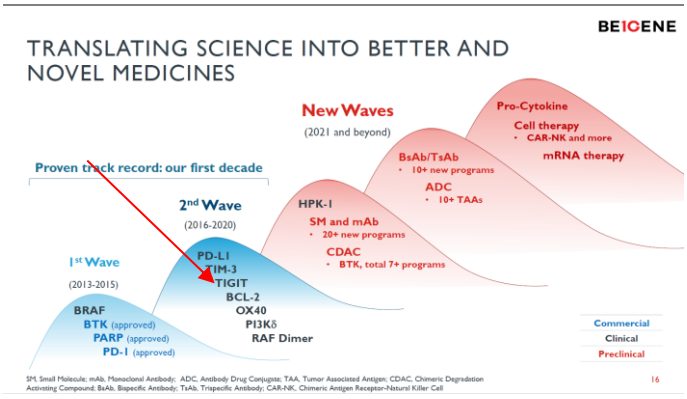
Exhibit 48. Pipeline summary of Chinese biopharma's & biotech's

	BEIGENE	Zai Lab	RemeGen	JUNSHI	Innovent	Legend	Akeso	HENGRUI	KeyMed
Ticker	BGNE US	ZLAB US	9995 HK	1877 HK	1801 HK	LEGN US	9926 HK	600276 CH	2162 HK
Current selling drug	2	4	2	3	7	1	2	11	0
Pivotal/after drugs in pipeline	2	9	2	3	7	3	5	17	0
Among which:									
Biosimilars	0	0	0	2	1	0	0	0	NM
License in's	1	9	0	1	5	0	0	0	NM
Pivotal/after indications	4	15	4	3	12	0	13	32	NM
Pivotal/after combinations	10	0	1	10	26	0	9	37	NM
Already approved by FDA	0	2	0	0	0	0	0	0	NM
Revenue driving in late-stage pipeline	Ociperlimab (BGB-A1207)	Repotrectinib (TPX0005)	RC28	Ongericimab (JS002)	Tafolecimab (IBI 306)	NA	Cadonilimab (AK104)	NA	NA
	Sotorasib (AMG510)	Adagrasib (MRTX849)					Ivonescimab (AK102)		
	Zanidatamab								
Total active clinical trials	95	15	32	82	102	14	72	446	16
Among which: out of China	54	8	4	5	7	4	7	11	0
Early-stage by drug									
In-house									
ADC	0	0	6	1	1	0	0	5	1
PROTAC (BTK CDAC)	1	0	0	0	0	0	0	1	0
BsAb (双抗)	0	0	5	0	4	0	1	0	2
Fusion protein	0	0	2	1	0	0	0	2	0
CAR-T	0	0	0	0	0	7	0	0	1
PARP	1	0	0	0	0	0	0	1	0
PCSK9	0	0	0	0	1	0	1	0	0
S-Protein (COVID)	0	0	0	1	1	0	0	0	0
mAb (单抗)	8	0	1	7	6	0	7	15	4
Others (inhibitors)	1	0	1	6	5	0	0	25	3
Subtotal in-house	**11**	**0**	**15**	**16**	**18**	**7**	**9**	**48**	**11**
License-in/co-development									
ADC	2	0	0	1	1	0	0	0	0
PROTAC (BTK CDAC)	0	0	0	0	0	0	0	0	0
BsAb	2	4	0	5	0	0	0	0	1
Fusion protein	1	0	0	0	0	0	0	0	0
CAR-T	1	0	0	0	1	0	0	0	0
PARP	0	0	0	0	0	0	0	0	0
PCSK9	0	0	0	0	0	0	0	0	0
mAb	9	6	0	4	1	0	0	0	2

Others	5	4	0	5	3	0	0	0	0
Subtotal licensed-in	**20**	**14**	**0**	**15**	**6**	**0**	**0**	**0**	**3**
Early-stage total	**31**	**14**	**15**	**31**	**24**	**7**	**9**	**48**	**14**

Source: ZLAB, BGNE, Innovent, JUNSHI, HENGRUI, Akeso, Legend, HENGRUI, SinoBio, Clinicaltrials.gov, Blue Lotus (2022/10/21). Information as September 11, 2022, excl. suspended, terminated, withdrawn and completed trials.. UD=Undisclosed

Exhibit 49. Illustration of evolution by BGNE



Source: BGNE (2021), Blue Lotus (2022/10/21)

Exhibit 50. Pipeline players in key fields

	ADC	PROTAC	BsAb	CAR-T
Listco players	RemeGen, BGNE, LEPU, HENGRUI	BGNE, HENGRUI, SinoBio, Kintor, Hinova, Haisco	Akeso, BGNE, Innovent, KeyMed	LEGN, CARsgen, Gracell, Immunotech, JWT, FOSUN
Startup players	DAC	Kangpu, Ranok, Accutar, Cullgen	Epimab, Biotheus, ImmuneOnco	Bioheng, BioRay, IASO
Total drugs post IND	30+	10+	50+	30+

Source: Pharmaprojects, Blue Lotus (2022/10/21)

ADC/PROTAC/BsAb, CAR-T and BsAb are new areas of focus

ADC, PROTAC, Fusion Protein and BsAb are all dual structures of different entities.

ADC drugs are heatedly contested: ADC leader RemeGen has 6 drug candidates in its early-stage pipeline, while HENGRUI has 5; Innovent, JUNSHI and KeyMed has 1 each. ADC competition which has filed for IND include LEPU (5), DAC (4), Kelun Botai (2), QILU (2), FDZJ (1), Biocytogen (1), LaNova (1), etc. There are at least 30+ ADC drugs filed for IND in China, based on our estimate. CDMO's like Wuxi XDC and SinoBio have filed for ADC patents believing they can license linker and manufacturing for a fee;

PROTAC drugs are developed by BGNE, HENGRUI and SinoBio in house. Kintor (9939 HK, NR), Hinova (688302 CH, NR), Haisco (002653 CH, NR) and several biotech startups, including Kangpu (康朴), Ranok (珃诺) and Accutar (冰洲石) have drugs in early-stage trials,. PROTAC links two small molecules while ADC links one big and one small. Fusion Protein and BsAb link two big molecules. We estimate there are 10-15 PROTAC drugs in the post IND pipelines of the companies.

BsAb will see competition between Akeso, BGNE and Alphamab.

BsAb (Bispecific Antibody) engages two disease targets within one molecule. Comparing to the combined usage of two mAb's, BsAb can reduce the side effects and give better efficacy. Further, BsAb has been the follow-on development path for most mAb's. Akeso's Cadonilimab (AK104) is the first domestically developed BsAb approved and the 3rd BsAb approved to sell in China. Amgen's BsAb Blinatumomab (*Blincyto*) is commercialized in China by BGNE treating Leukemia and

Roche's Emicizumab (*Hemlibra*) was sold by Roche to treat Haemophilia A. Cadonilimab treats Cervical Cancer as its first approved indication. We expect Cadonilimab to substantially grow in sales in 2023 following the entry to NDRL. Akeso has two more BsAb's in Phase II/III, AK112 and AK101 while BGNE's licensed BsAb from Zymeworks, Zanidatamab (ZW25), is now in global Phase III and just licensed to Jazz Pharmaceutical. Another company with late stage BsAb is Alphamab (9966 HK, NR). Its PD-L1/CTLA-4 BsAb (KN046) and HER2/HER2 BsAb (KN026) are both in Phase II/III. Innovent has 4 BsAb (JS322, 323, 363, 389) in house in early stage. JUNSHI partnered with Revitope (private) for 5 BsAb's but seems to be lacking candidate in-house. KeyMed has two BsAb (CM336, 350) in the early stages. Startup developers include Epimab (岸迈) which has 6 BsAb's in early clinical. Biotheus (普米斯) has 6 BsAb's passing IND and ImmuneOnco (宜明昂科) has 3 BsAb in early clinical. In total we estimate there are 50+ BsAb drugs in various post-IND, early stages at this point. F-Star Therapeutics, which faced extended security review for its acquisition by SinoBio, has 3 post-IND BsAb in its pipeline. If SinoBio, an early partner to Akeso, successfully completes the acquisition, it will become a meaningful player as well.

ADC and CAR-T each have ~30 drugs in the post-IND-to-early-clinical stages.

Fusion Protein is similar in structure to BsAb but is not confined to antibodies. Fusion Protein drugs scatters in various pipelines of RemeGen (2), HENGRUI (2) and JUNSHI (1) as well as BGNE (1).

Cell therapy as the latest wave of drug making technology has caught the attention of many and is in the transition from academia and license-in to in-house among many Chinese innovative drug developers. LEGN is the domestic leader with the 2nd BCMA-targeted, 6th overall CAR-T therapy approved by FDA. LEGN works with Johnson & Johnson in the US for this therapy (*CARVYKTI*) and now has 7 CAR-T therapies under trial targeting BCMA, CLDN 18.2, CD19/20/22 and GPC3. LEGN split profit 50:50 for CARTYKTI outside of China and 70:30 inside China with J&J. CARsgen (2171 HK, NR) has 2 CAR-T in Phase II/III and another 5 in Phase I, targeting BCMA, CLDN 18.2, GPC3 and CD19. Gracell (GRCL US, NR) has 5, 2 of which are Universal CAR-T (UCAR-T) and Immunotech (6978 HK, NR) has 3 at the early-stage. In the licensed-in camp, JW Therapeutics has 7 CAR-T in the pipeline licensed from Eureka and BMS. FOSUN Kite has all pipeline from Gilead Kite. Among listco's, BGNE and Innovent each has 1 license-in CAR-T's from Amgen and Roche, respectively. Startup CAR-T companies include Bioheng (3), Bioray Lab (3), IASO (3), CBMG (3), PersonGen (1) and TCR-T (T-cell Receptor) company Xlifesc (香雪生命). We estimate there are also at least 30+ CAR-T drugs in the post IND, early clinical stage.

Chinese are leading in BsAb and CAR-T with global first coincide with Chinese first.

According to <*The Clinical Pipeline for Cancer Cell Therapies*> (S. Upadhaya, et.al, *Nature Reviews*, July 2021), China and US led in global cell therapy developments with 695 and 791 projects ongoing by April 2021 vs. 498 and 605 in 2020. In April 2021, there were a total of 2,073 cell therapies under development worldwide.

China and US dominate global cell therapy research but in China many such research is still in the academia and startups. We expect them to be commercialize soon.

The split in China between academia and industry was 47/53 in 2020 but has since changed to 40/60 in 2021, while the ratio in US was 21/79 in 2020 and since moved to 17/83 in 2021, according to the above research. This suggests that cell therapy is still at the early stage of commercialization. US leads China in commercialization but China is commercialize more. We will likely see more CAR-T and other cell/gene therapy research move from academia to industry in the next few years, adding competition to LEGN.

PARP inhibitors and **PCSK9 inhibitors** have also attracted some concentrated pipeline interests mainly due to global success and therapeutic needs. BGNE and HENGRUI each have 1 PARP inhibitors in their early-stage pipelines. JUNSHI has 1 licensed-in (JS109). There are three PARP inhibitors on the market treating breast cancer in China: (1) ZLAB's flagship selling drug Niraparib (*ZEJULA*), (2) HENGRUI's Fluzoparib (selling) and (3) AstraZeneca's Olaparib (selling). However, the recent recall by three PARP makers in the US, including *ZEJULA*, might impact the prospect of PARP Inhibitor worldwide.

Small molecule inhibitors have been revenue drivers for the pre-PD-1/L1 generation of innovative drug makers and still so for HENGRUI, BGNE and SinoBio.

PCSK9 is a big molecule enzyme that can lower cholesterol levels which can treat affected patients globally. Innovent and Akeso have 1 each in their early-stage pipelines. But this category also has several late-stage candidates include HENGRUI's SHR-1209, JUNSHI's JS002 (Ongericimab), Innovent's IBI306 and Akeso's AK102 (Ebronucimab), competing against successive generation of Statin type drugs. We believe PARP and PCSK9 are niche markets as PARP is confined to breast cancer and PCSK9 has many competing products for a clinical demand that is not life critical.

BGNE and Innovent are the most determined growth seekers

BGNE's small molecule drugs had successful in-house discoveries like Zanubrutinib (*BRUKINSA*). Yet its big molecule antibody drugs also have successful in-house hitters like Tislelizumab (PD-1) and Ociperlimab (TIGIT). This is similar to HENGRUI's successes in Apatinib Mesylate (TKI) and Camrelizumab (PD-1). Similarly, SinoBio is also seeking such a transition. Its PD-1/L1 drug, Penpulimab, co-developed with Akeso, hasn't been a hitter. But its small molecule MTKI (Multitarget Tyrosine Kinase Inhibitor) Anlotinib has generated Rmb3-4bn revenues a year.

After embarking on the journey to biopharma, undisrupted growth becomes the first priority. Therefore, both BGNE and Innovent must fill the pipeline to sell. BGNE is ready. Innovent, in our opinion, is not.

So, in terms of timing to launch the transition to a product-sales-driving biopharma different companies have different answers. We saw JUNSHI's license-in strategy, for example, increasingly turning to local biotech startups and academia. Among JUNSHI's 11 licensed-in/co-developed drugs in its early-stage pipeline, 4 (JS110, 111, 112 and 113) are from Wigen Bio (微境生物), 2 (JS 104 and 105) are from Risen Pharma (润佳医药), 1 each (JS108, 018, 019) are from DAC Biotech (多禧生物), Enrini Biotech (恩瑞尼生物) and Leto Labs (志道生物) and 1 (JS501) is a biosimilar from a subsidiary of generic drug maker Huahai Pharma (600521 CH, NR). JUNSHI's COVID drug Etesevimab (JS016) is co-developed with the Institute of Microbiology under the Chinese Academy of Sciences. We believe the kind of drugs in sales affects the kind of salesforce recruited. Over time it also positions the company differently.

We like RemeGen and Akeso because they don't insist on turning to biopharma with a set timetable regardless of circumstances and environments. In our view, with NDRL firmly in place, CDE/NMPA tightening on the horizon and US-China trade friction likely spread to biotech, the go-slow approach seems to make more sense. In a go-slow approach, a biotech uses license-out to pay for its R&D until it accumulates more than two mini-blockbuster drugs (<Rmb1bn in annual sales) to kick off its transition to a biopharma.

We believe RemeGen and Akeso's approaches to biopharma have a higher chance of success.

Competition is inevitable…Leverage competency is the key

In 2022, a total of 20,109 drug candidates are undergoing clinical trials, up 8% from 2021 and up 35% from five years ago (*Source: Pharmaprojects*). Among these drugs, 86% are in the early stages (Preclinical to Phase II), 5.6% are in Phase III and 8.2% are in the commercialization process. This means more than 90% of all clinical trials are doomed to fail (Exhibit 51).

Chinese innovative drug developers lean their development efforts on cancer and cardiovascular diseases, two leading causes of death in China.

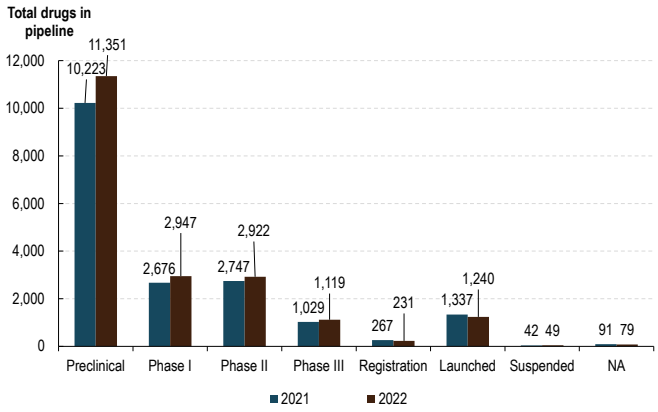
Global therapeutic areas overlap

Globally oncology accounts for <40% of clinical trials and <30% of drugs under development (Exhibit 52). Figures in China are higher. Another therapeutic area where China develops more drugs than global average is Cardiovascular.

With a few exceptions, the top causes of death in China are similar to those in the US and the World. According to World Life Expectancy, Gastric Cancer is the 5th cause of death in China but only 33rd in the US. Esophagus Cancer was the 10th cause of death in China but only 28th in the US. This is probably diet related. On the contrary, Alzheimer & Dementia is the 2nd cause of death in the US but only 6th in China. Kidney Disease is the 6th cause of death in the US but only 11th in China. Citizens in both countries aren't expected to die from Influenza and Pneumonia, Diarrheal Diseases and Tuberculosis, even though they are the 4th, 7th and 12th causes of death worldwide. This is probably related to sanitation.

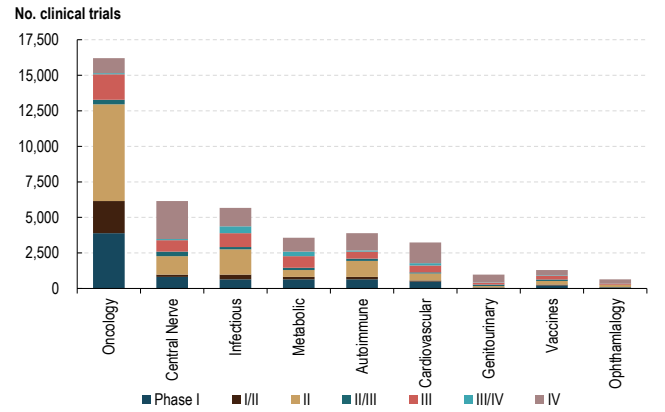
These show that the therapeutic profile of Chinese does contain a few peculiarities. But the majority of therapeutic areas do overlap. Out of the top 20 causes of death in China, 15 also show up in the top 20 in US and 12 also show up in the top 20 worldwide (Exhibit 53).

Exhibit 51. Global drug candidates count



Source: Pharmaprojects, Blue Lotus (2022/10/21)

Exhibit 52. Global clinical trials count



Source: Pharmaprojects, Blue Lotus (2022/10/21)

China's fundamental research catches up but so did a few others

According to SCImago, a service that tracks scientific papers, citations for published scientific papers from China in a given year has grown from No. 6 in the world in 2010 to No. 4 in 2012, No.3 in 2015 and No.2 in 2018. Adjusted citation (less self-citation) as percentage of US rose from 20% in 2010 to 60% in 2021. In terms of published scientific paper pertaining to biotech fields (Biochemistry, Genetics, Immunology, Microbiology and Molecular Biology), the trend is similar (Exhibit 54). China has surpassed Japan in 2012, Germany in 2016 and UK in 2017.

China's fundamental research is improving the fastest, but others non-US countries also.

The index of SCImago measures the quality of scientific papers based on the number of citations they received in the years after publishing. It therefore shows China's quality of published scientific papers have improved continuously over time.

The same, however, is also happening with countries like India, Italy, Australia and Brazil, at least in the biotech fields. Biotech paper citations from these four countries rose from 41% of US in 2011 to 80% in 2021 (Exhibit 54). Further, UK, Canada, Germany, France, Spain, Netherland, Japan and Switzerland remain significant but stable contributors of fundamental research in biotech. Biotech paper citations from these eight countries rose from 170% of US in 2011 to 202% in 2021.

More fundamental researches are being published out of US. Countries and corporations who can provide a commercialization platform for these research will win. US, with 40% of global pharmaceutical market, is the leading choice.

Overall, the dominance of US in scientific paper citation is waning, overall and in biotech. The good news is there will be an increasing inflow of commercializable research from Chinese academia to industry in the years to follow. The caveat is that an increasing portion of good research is also available in in other non-US countries. Countries and corporations who can provide a commercialization platform for these scientific discoveries in these countries will win. So far, with the biggest pharmaceutical markets in the world by a wide margin, such platform still belongs to USA.

Cash will play an increasingly important role in competition

China's biotech sector has ballooned to ~66 companies over the past three years. But a lot more will come to the market.

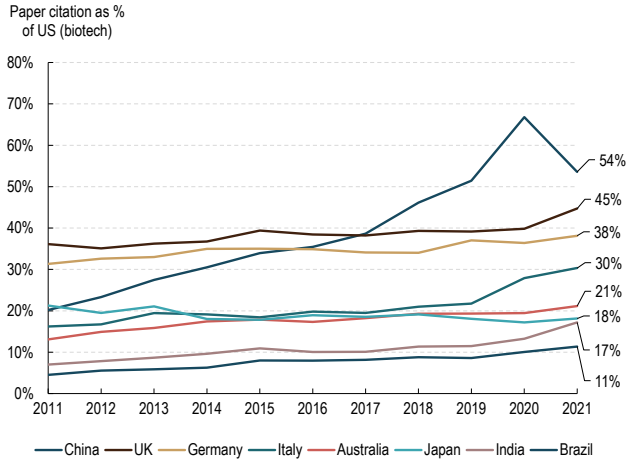
Since HKSE set out lowered listing requirements for biotech companies in Section 18A of the <*Main Board Listing Rules*> in August 2018, there has been a listing of 52 biotech companies, among which there are 2 dual listing (BGNE and ZLAB) and 14 medical device companies. The remaining 36 biotech companies raised a total of HK$76bn (US$9.7bn), or HK$2.1bn (US$269mn) each. Besides relistings, the top fund raisers were RemeGen, Everest, Innovent, KeyMed (2162 HK, NR), JUNSHI and Henlius. Further, BGNE, RemeGen, JUNSHI and CanSino have listed themselves in the A-share Science and Technology Innovation Board (STAR) and more are coming. By September 2022, a total of 93 biotech/device/diagnostic companies have listed on the STAR SSE, among which 26 were biotech companies.

So far, the STAR SEE has a stringent track record of accepting re-listings from Nasdaq and HKSE. If that changes, more biotech's can escape death.

Exhibit 53. Causes of death ranking

	Word	China	US	Japan
Coronary Heart Disease	1	2	1	1
Stroke	2	1	4	2
Lung Disease	3	3	3	5
Influenza and Pneumonia	4	12	11	3
Lung Cancers	5	4	5	4
Alzheimer & Dementia	6	6	2	7
Diarrheal diseases	7	50	37	37
Diabetes Mellitus	8	14	10	29
Kidney Disease	9	11	6	9
Liver Disease	10	15	16	17
Gastric Cancer	16	**5**	33	8
Esophagus Cancer	26	**10**	28	20
Colon-Rectum Cancer	14	**9**	**9**	**6**
Hypertension	13	**7**	**8**	28

Exhibit 54. Biotech paper citation as percentage of US



Source: WHO, Blue Lotus (2022/10/21)

Source: SCImago, Blue Lotus (2022/10/21) *Citation deducts self-citation. **Biotech includes biochemistry, genetics, microbiology, immunology and molecular biology fiends Blue Lotus (2022/9/7)

Success of biotech depends on a very big denominator

We count ~784 biotech companies traded on Nasdaq, among which 637 was headquartered in the United States, some further 27 on NYSE and 77 on OTC (*Source: Topforeignstocks*). The Nasdaq Biotechnology Index (NBI) contains 365 stocks..

We believe that with US-China rivalry spreading from semiconductor to biotechnology, more Chinese biotech IPO's will head to HKSE or STAR markets.

Biotech's with below average quality will likely face cash shortage soon. But good quality biotech's do not seem to have fund raising issues.

Low liquidity of biotech's on HKSE means most will not raise money again

We found that out of the 36 HKSE-18A biotech's listed, only 7 stocks had a 3M trading volume more than US$5mn a day in late September. Sixteen had trading volume less than US$1mn a day. If the stringent requirement of dual listing on STAR SEE persists, HKSE-18A stocks will likely face challenge from raising capital again. This will lead to more low-quality biotech's to try to go to STAR SSE for listing. But for those with proven track record fund raising from multiple markets seems not be to a problem, as relistings for BGNE, RemeGen, Innovent and ZLAB have shown.

The global and China venture capital investments have also slowed down in C1H22 but China is fetching better than global (Exhibit 55 and 56). We believe this is due to the solid fundamentals of investing in China's biotech fields amid the breakthroughs in immunology oncology, genetics and cell therapies in the latest decade, which China has indeed leapfrogged. Some Chinese biotech's are capable of developing global FIC drugs now. Scientists of the Chinese descent participated in biotech research for a decade up to its breakthrough point and many are now returning to China to start a biotech company. Chinese government has proactively promoted life science educations since the 1980's. Most leading Chinese universities established colleges of life science in the 1980's to 1990's, producing a large quantity of educated labor in this field.

Global biotech venture investments are leanings towards China.

Exhibit 55. Global and China venture investment in biotech

(US$ bn)	2016	2017	2018	2019	2020	2021	1H22
Amount (US$ bn)							
Global	10	15	29	28	42	58	20
China	1.5	1.9	6.9	5.0	13	17	5.9
China %	14%	13%	24%	18%	31%	29%	30%
Deals							
Global	608	702	935	929	1,110	1,445	568
China	377	476	585	640	724	844	314
China %	62%	68%	63%	69%	65%	58%	55%
Deal size (US$ mn)							
Global	17	21	31	30	38	40	35
China	4.0	4.1	12	7.9	18	20	19
China %	23%	19%	38%	27%	47%	51%	53%

Source: VBDATA, Blue Lotus (2020/10/21)

Exhibit 56. Venture investment in biotech

	1H17	1H18	1H19	1H20	1H21	1H22
Amount (US$ bn)						
Global	5.6	16	13	18	32	20
China	1.0	4.6	2.3	3.8	7.8	5.9
Amount YoY						
Global	22%	180%	(15%)	33%	76%	(37%)
China	33%	386%	(49%)	64%	104%	(25%)
Deals						
Global	326	460	161	498	731	568
China	291	354	106	228	359	314
Deals YoY						
Global	4.2%	41%	(65%)	209%	47%	(22%)
China	38%	22%	(70%)	115%	58%	(13%)

Source: VBDATA, Blue Lotus (2020/20/21)

Duplication of R&D is still a problem but sheer number does push up quality

In 2021, CDE/NMPA approved 1,310 chemical-based Investigative New Drug (IND) applications, of which 49% was Oncology; 764 Biological Drug Applications (BDA), of which 59% was

Scientists of the Chinese descent participated in biotech up to its breakthroughs and many then returned to China to start a biotech company.

Oncology and 44 Traditional Chinese Medicine (TCM) drug applications, of which none was Oncology (Exhibit 57).

For comparison we estimate FDA received 700-800 IND each year except in 2021, when there was a surge of COVID-related submissions. So China is receiving more on average.

Of the 304 Oncology IND applications that continued to clinical trials, 92% were concentrated in the top five targets: PD1/L1 (43%), HER2 (14%), EFGR (14%), VEGFR (12%) and CD-3 (9%), as shown in Exhibit 58, which does indicate research efforts in China are very concentrated.

The majority of improvement still comes in sheer numbers, but there is slow improvement in quality as well.

The crowded development, however, does come with quality improvements. According to <Evolution of innovative drug R&D in China>, *Nature Review*, April 1, 2022, out of 1,147 drugs the authors tracked up to July 2021, 292 (26%) was first-in-class (FIC), 338 (29%) was fast follower (FF) and 517 (45%) was me-too (MT), comparing to 197 (27%), 166 (23%) and 365 (50%) in 2020 (Exhibit 60). There are improvements in both absolute numbers as well as weight in FIC+FF.

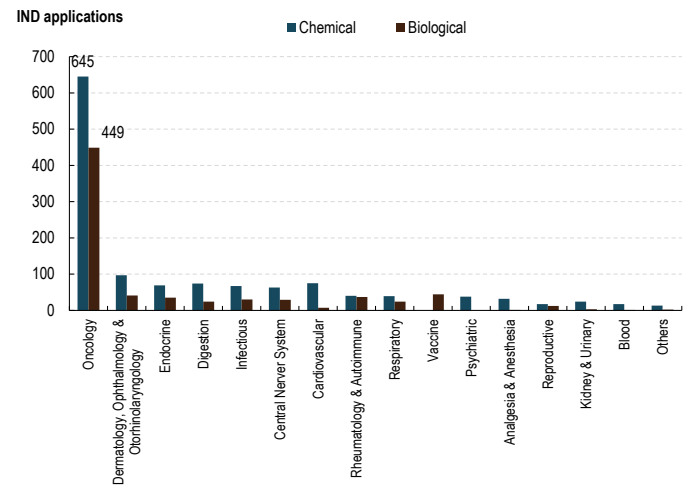
As shown in Exhibit 59, HENGRUI, SinoBio, JUNSHI, Innovent and BGNE are among China's top filer of innovative drug applications. China's generic and drug supply chain companies also continue to pile into innovative drug development, leveraging their size. IND filings by Haosoh (豪森药业) went from zero in 2019 to 15 in 2021. FOSUN Pharma filed 13 IND in 2021, up from 3 in the prior year. From 2020 to 2021, the number of IND applications doubled from 59 to 125.

2021 saw 2x filing of IND from top 10 innovative drug makers.

But there were exits, too. GD HEC (1558 HK, NR) saw filings decline and SIMM of CAS (Shanghai Institute of Materia. Medica. of Chinese Academy of Science) exited the market in 2021. The transition from generic to innovative has high fatalities.

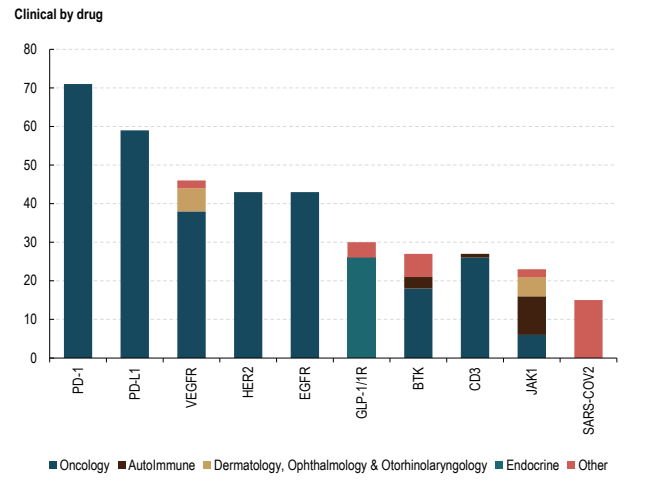
Further, specialized innovative drug developers like RemeGen, Akeso and LEGN do not submit a lot of IND's, as shown in Exhibit 59.

Exhibit 57. CDE IND applications by indications, 2021



Source: VBDATA, Blue Lotus (2020/10/21)

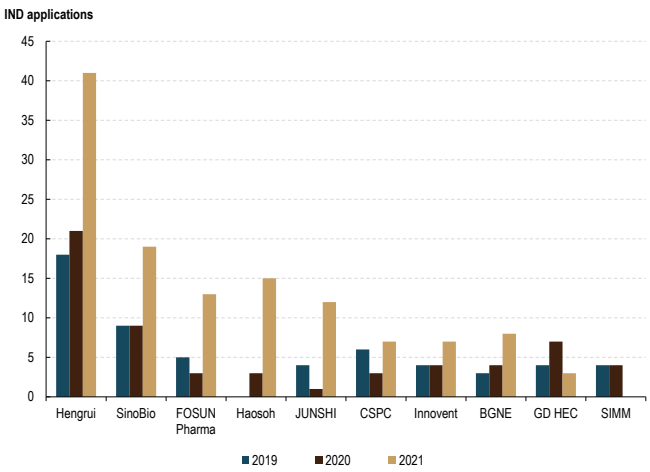
Exhibit 58. Clinical trials by drug, indication & target



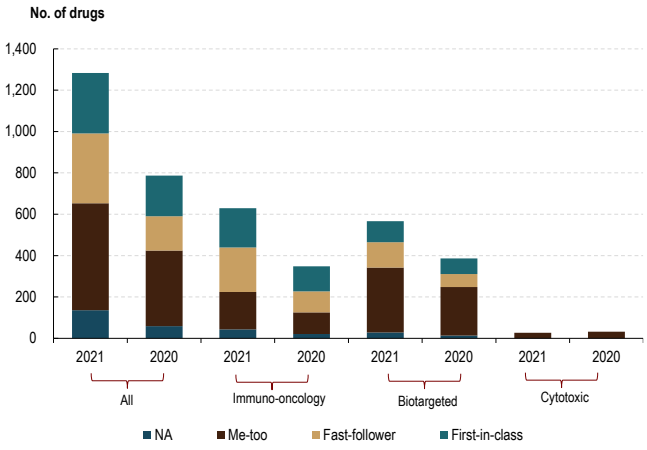
Source: VBDATA, Blue Lotus (2020/20/21)

Exhibit 59. CDE IND applications by companies, 2021

Exhibit 60. Improvement in innovative drugs in China



Source: CDE, Blue Lotus (2020/10/21)



Source: Nature Review, Blue Lotus (2020/20/21)

It is too early to talk about survival, but cash is affecting business

Exhibit 61 shows the net cash (cash less debt) positions of leading innovative drug developers. We divide their C2Q22 net cash positions by the average free cash flow in the previous two years to arrive the number of quarters these developers can last assuming the same free cash flow continues. We pick a two-year horizon for the availability of audited data, as well as for factoring in the impact of royalties and milestone payments. It acts as a rough measure for cash adequacy of the companies.

BGNE has amassed enough cash to incur 4-10x free cash outflows of its peers.

Cash situations vary from company to company

We found the leading innovative drug developers, like BGNE, ZLAB, HENGRUI, RemeGen and Innovant keep 11-15 quarters worth of free cash flow on hand. Despite BGNE's free cash outflow being the biggest, reflecting its long-standing strategy of pursing a global standard in R&D, its cash position still reached 13 quarters. This is despite that BGNE's R&D cost is bigger than our next six covered company combined. On the other hand, despite HENGRUI having consistently positive operating cash flows from its generic business, its investment cash outlay has risen sharply recently, reflecting the pressure of transition is immense.

Some innovative drug developers are certainly facing liquidity problems, despite their market capitalizations and trading volumes remained decent. Akeso, Henlius and LEPU are three with only less than two quarters of free cash flow left on its account. Henlius, in particular, has more debt than cash, showing itself as having a negative net cash balance.

Akeso, Henlius and LEPU have little cash left on their accounts.

Exhibit 61. Cash and cash flow situations of biotech's

(US$ mn)	BEIGENE	Zai Lab	HENGRUI	RemeGen	LEPU	Henlius	Innovent	JUNSHI	Akeso	KeyMed	InnoCare	Legend	CARsgen
Ticker	BGNE US	ZLAB US	600276 CH	9995 HK	2157 HK	2696 HK	1801 HK	1877 HK	9926 HK	2162 HK	9969 HK	LEGN US	2171 HK
Therapeutic area	Multi-front	Multi-front	Multi-front	ADC	ADC	Immuno-oncology	Imm.-onc..	Imm.-onc.	Imm.-onc.	Imm.-onc.	Imm.-onc.	CAR-T	CAR-T
R&D model	Mixed	License -in	In-house	In-house	In-house	In-house	In-house	In-house	In-house	In-house	In-house	In-house	In-house
C1H22 net cash	5,138	1,267	2,825	490	60	(427)	1,139	515	140	490	761	635	384
Average interim FCF	(802)	(238)	(370)	(82)	(61)	(118)	(215)	(161)	(120)	(30)	(29)	(133)	(57)

No. of quarters last	**13**	**11**	**15**	**12**	**2.0**	**NM**	**11**	**6.4**	**2.3**	**32**	**52**	**9.5**	**13**

Source: BGNE, ZLAB, HENGRUI, RemeGen, LEPU, Henlius, Innovent, JUNSHI, Akeso, KeyMed, InnoCare, Legend, CARsgen, Blue Lotus (2022/10/21).

We understand that several reasons can shed a different light:

- **Parent support might show up**: Both Henlius and LEPU are subsidiaries of larger corporate parents FOSUN Pharma Group and LEPU Medical;
- **Listing on STAR SSE** might be delayed for exogenous reasons, depriving opportunity to raise capital, but might eventually arrive. We understand Henlius falls into this category;
- **Company has pending commercialization**. Akeso's PD-1/CTLA4 bispecific antibody (BsAb) Cadonilimab (AK104) received CDE approval on June 24, 2022 and became the first domestically developed BsAb and the six globally. Company stated it intended to grow Cadonilimab sales to the level of Rmb1bn a year in its first year.

Everest seems to be selling ADC drug back to Gilead after three years at a loss in order to conserve cash.

On August 16, 2022, Everest Medicine (1952 HK, NR) sold the Asian rights (incl. China) of *Trodelvy*, the 4th selling ADC drug in the world, back to Gilead for a total consideration of US$455mn. In April 2019, Everest licensed *Trodelvy* from Gilead in a deal valued at US$835mn in total. The deal added Rmb86mn, Rmb476mn and Rmb866mn in intangible purchases on its cashflow in 2019-21 and impacted Everest's cash position. We believe part of Everest's decision has to do with strong performance of *Erhertu* (Daiichi Sankyo/AstraZeneca) and other ADC drugs in the pipelines of various developers. But also, part of the decision has to do with a cash flow. As of C1H22, Everest had a net cash position of US$299mn but a two-year-average-interim free cash outflow of US$122mn, meaning its net cash can sustain less than five quarters of unrestrained operations.

KeyMed and Innocare have ample cash on hands but we don't find bright spots yet in their pipeline.

On the other hand, KeyMed and InnoCare seems to have excessive cash on their balance sheet and both of which have incurred very low level of cash outlays among peers. We understand KeyMed's situation might be due to its founder carrying significant knowhow from its previous employer JUNSHI. We understand InnoCare's pipeline remains early stage so large amount of late clinical trial cost might be still to come. But the cash strategy of these two firms might also reflect these two companies' view on the overall market. Currently we do not see bright spots in the pipelines of these two companies. We might reevaluate if they make pipeline acquisitions in the quarters to come.

It is too early to talk about survival

Local Chinese banks can provide soft loans under the policy umbrella of supporting innovation.

Despite cash shortfalls, we believe it is premature to talk about survival of Chinese biotech's. Through listing on STAR SSE, selling off assets and pipelines, mergers and acquisitions and bank loans we believe more Chinese biotech's can receive more funding. Most of Chinese biotech's receive government grants anyway.

On a macro viewpoint, China has the largest patient population in the world. Each year 4.6mn cancer cases develop, according to IARC, 24% of the global total. Each year 3mn of Chinese die of cancer, 30% of the global total as of 2020.

On the demand size, there are huge unmet clinical needs. The 5-year cancer survival rate was only 41%, comparing to 66% in the US. According to Frost & Sullivan, chemotherapy accounted for 63% of China's cancer therapy market in 2020, comparing to the global average of 16%. Gastric Cancer and Esophagus Cancer are top causes of death in China but have not received adequate coverage from global pharmaceutical and biotech industries.

China's domestic market for innovative drug is huge as the government wants to drive out generic to make room for innovative drugs.

The history of China's innovative drug industry is short. It only started from 2015 to 2018 with the consistency evaluation of the generic drug industry, i.e., evaluating whether the generic drugs produced were what their labels said they were. The reform gained momentum from the expansion of national health insurance scheme to the rural population, crossing 50% national coverage for the first time in 2017. These two reforms paved the ground for innovative drugs to take the place of generic in doctors' prescriptions, with a funding source to pay for it. The launch of NDRL and centralized procurement from late 2018 further squeezed the generic drug industry to make room for innovative drug but also shortened the life cycle of the latter.

On the supply side, China's talent pool for life science is huge.

- **American universities award ~1,000 life science PhD's to Chinese nationals each year**: According to NCSES of NSF, 52.5K Chinese nationals received their PhD's from science and engineering programs of American universities from 2010 to 2020, 39% of all foreign nationals receiving such degrees and 15% of all science and engineering PhD's awarded. About 27% of science and engineering PhD's are awarded to life science, which translates to ~14.2K Chinese nationals received life science PhD's from American universities from 2010-20, or ~1.2K per year. Adding PhD's awarded to Chinese nationals in EU, Japan and Oceania, we estimate annual PhD's awarded to Chinese nationals can easily top 2,000;

Chinese nationals took 39% of all science and engineering PhD's awarded to foreigners and 15% of total from American universities.

- **Chinese universities award ~10,000 life science PhD's at home each year**: According to CSET, China produced 9,668 life science PhD's in 2019. In 2019, China awarded 49K science and engineering PhD's, outpacing US by 47%. China has been awarding more science and engineering PhD's than US has done since 2007;
- **Chinese universities awards ~100K life science masters each year**: Based on figures released by MOE, we estimate the number of life science masters to be ~10x of the PhD recipients.

Today the overseas returnees, acting as researchers, entrepreneurs and managers and armed with global pharma/biopharma work experience, work with domestically educated PhD's, master's and bachelor's to form an ecosystem of talents. The supply side story is equally compelling.

With demand and supply both in China's favor, we believe China's innovative drug industry should grow at least 4-6x to become 25-30% of the US.

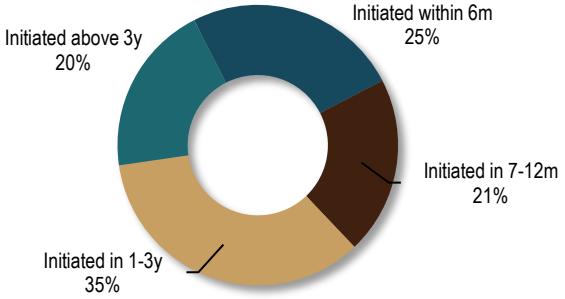
With both the demand and supply side in favour of China, we believe it is likely China's biotech industry will develop into 25-30% of the size of the US. In 2019, according to data compiled by USCES, China's biotech industry only constituted 4.2-5.6% of the US. As a result, we believe China's innovative drug industry has room to grow at least 4-6x in a foreseeable future. Under this scenario we believe cash shortage is short term in nature and should not hinder investor's judgment in this sector.

Relief of clinical resource shortage proved the point

Due to intense competition, crowded R&D in high-profile cancer indications and COVID, clinical trials in China ran into a glut in 2020 but in 2021 was quickly relieved. The percentage of clinical

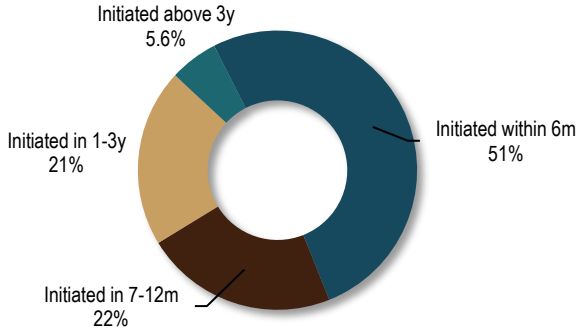
trials that initiated patient recruitment within 6 months after IND more than doubled to 51.4%. Percentage of clinical trials not initiated within 3 years (backlog) decreased to 5.6% (Exhibit 62 and 63).

Exhibit 62. Initiation time for clinical trial start in 2020



Source: CDE, Blue Lotus (2022/10/21)

Exhibit 63. Initiation time for clinical trial start in 2021



Source: CDE, Blue Lotus (2022/10/21)

Consolidation in R&D and organization in order

We believe in the next 6-12 months a negative drag to the sector is the converging force of a more stringent CDE in fast tracking approvals and a STAR SSE market that is liberal in admitting IPO's.

A double supply hit is on its way…It will deflate the sector valuation

2022 YTD approval data from CDE showed slowing approval for domestically developed innovative drugs and accelerated approval for imported drugs.

As aforementioned, the development of China's innovative drug industry started from 2016, in which year CDE approved, for the first time, 7 innovative drugs, of which none was Accelerated. Since then, CDE's approval speed accelerated to 283 drugs in 2021, of which 99 was Accelerated Approval. However, heading in 2022 there are signs that CDE's approval pace has slowed down. Further, the pace for approving imported drugs has quickened (Exhibit 64).

Exhibit 64. Innovative drug approval by CDE has slowed down in 2022

	Type 1	Type 2	Type 5	Chemical (1+2+5)	Biologics	Innovative drug total	Standard approval	Accelerated approval
Definition	Not marketed anywhere and original	Not marketed anywhere but modified	Imported	Small molecule	Big molecule			
2016	-	-	7	7	-	7	7	-
2017	8	2	29	37	2	39	9	30
2018	12	18	65	101	7	108	72	36
2019	24	14	50	78	10	88	56	32
2020	50	78	67	171	24	195	128	67
2021	58	65	61	162	22	184	85	99
2022YTD	22	31	60	103	10	113	77	36

Source: CDE, Blue Lotus (2022/8/22). Type 3 and 4 are generic drugs.

By September 2022, only 22 Type 1 innovative drugs were approved. Total number of innovative drugs approved was 61% of 2021 but drugs approved under Accelerated Approval was 36%. This indicates CDE is approving less in Accelerated, favoring Standard now.

Further worth noting is the number of imported drugs (Type 5) reached 2021 level one quarter ahead in 2022.

More conservative new drug approval is a global trend

A crackdown on falsification has already quietly started, we believe.

As aforementioned, FDA has recently asserted that price was not a factor in its decision making. In reaching approval decisions, FDA follows the non-inferiority rule which states new drug approval must bring incremental clinical benefits, either in better efficacy, or lower toxicity, or new disease indications. Under such principle, FDA only approved 7 PD-1/L1 drugs while CDE, starting late approved 14. In February, 2022, a FDA panel rejected Innovent/Eli Lilly's application for Sintilimab on the ground it must run US-based clinical trials.

We believe CDE is following the lead of FDA now that there are enough PD-1/L1 drugs on the market to satisfy competition needs. In September 2022, industry sources suggested that Genor (6998 HK, NR) had let go its entire PD-1/L1 sales force. Genor's PD-1 drug Geptanolimab (GB226) applied for NDA with NMPA under Priority Review in August 2020 but more than two years later still hasn't been approved. In May 2022, Green Valley Pharmaceutical announced cancellation of its global Phase III trial for GV-971 for Alzheimer's disease. Rumour has been that GV-971's data was fabricated. Earlier GV-971 received CDE/NMPA's conditional approval on November 2019 and

received FDA's IND permission on April, 2020 and made it to the NDRL on April, 2022. We believe CDE will increasingly turn stringent in approving additional PD-1/L1 drugs with repeated indications as the existing drugs.

Standardizing process and improving quality are CDE's next stage priority

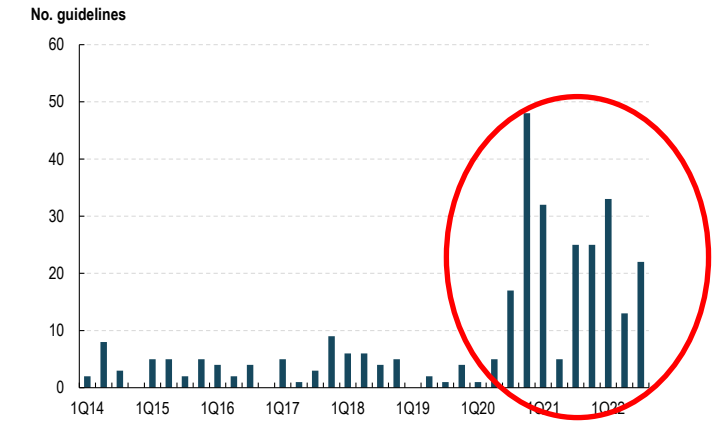
Since the kickoff of drug reform in 2015, adhering to international best practices of drug development has been a consistent theme. But we notice a pickup in activity starting from C2H20. In 2021/22, CDE/NMPA stepped up issuing various guidelines for the industry, with the important ones being:

Recent CDE guidelines are aimed at blocking shortcuts for drug developers to take advantage of the conditional approval process.

- On August 9, 2022, CDE issued three guidelines emphasizing on the need to put patient welfare first in conducting clinical trials. The <*Guidelines for the Design/Implementation/Risk-Benefit-Evaluation of Clinical Trials that Put Patients at the Centre*>, specified the principles company must abide in choosing placebo's in designing, implementing and evaluating clinical trials;
- On June 25, 2022, CDE issued the <*Guideline for the Change of Clinical Trial Designs*>, which specified incremental material submission and ethics review needed for material changes of clinical trial designs;
- On June 20, 2022, CDE circulated the draft version of the <*Technical Guideline for choosing Single-Arm-Test (SAT) for supporting the Approval Decision of Anti-Cancer Drugs*>, which has now finished review. It listed out 6 scenarios where SAT can be used over RCT (Randomized Control Test) for the conditional approval of oncology drugs, which means scenarios not in these 6 will not be approved;
- On November 19, 2021, CDE issued the <*Clinical Value-Oriented Guiding Principles for Clinical Research and Development of Anti-cancer Drugs*> with a stated aim to encourage differentiated innovation with therapeutic value while avoid over-crowdedness and wasteful use of clinical resources and funds.

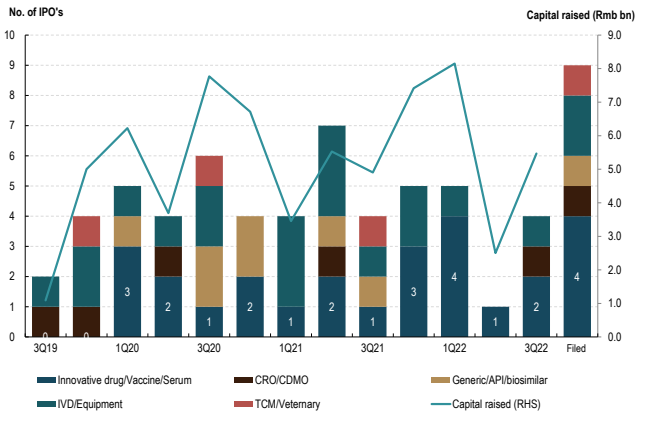
CDE's efforts at standardizing R&D through guidelines can help smooth Chinese innovative drugs' global push, but can also slowdown the approval pace.

Exhibit 65. No. of CDE guidelines issued



Source: CDE, Blue Lotus (2022/10/21)

Exhibit 66. Healthcare-related IPO's on STAR SSE



Source: STAR SSE, Blue Lotus (2022/10/21)

As Exhibit 65 shows, CDE issued 87 guidelines in 2021, up 71% from 2020. So far in 2022, CDE issued 46 with 22 finished reviews so at least 68 will be issued. CDE's issuance of guidelines picked up significantly starting from C3Q20.

26 biotech's raised Rmb40bn (US$6.1bn) since C3Q19 on STAR SSE, making STAR SSE an alternative IPO destination for Chinese biotech's.

Some of these guideline issuances have to do with China's joining ICH as a Regulatory Member. CDE intend to standardize the R&D process for innovative drugs development to be in-line with global best practices.

But STAR SSE has become a major source of listco supply

Removing dual listings which are mostly big names, there were 64 healthcare related stocks, including filed but not yet listed, on the STAR SSE market as of C3Q22, among which, 26 were biotech's, 20 were IVD (In Vitro Diagnosis)/Equipment, 8 were Generic/API/Biosimilars, 6 were CRO/CDMO's and 4 were TCM (Traditional Chinese Medicine)/Veterinary. Total capital raised was Rmb68bn, among which biotech's raised Rmb40bn (US$6.1bn). This compares to 35 biotech's (excl. dual listing) raising HK$76bn (US$9.7bn) on HKSE from C3Q18 till today. STAR SSE has already proven itself to be an adequate supply of exit liquidity for biotech startups in China.

Among the biotech's on STAR SSE, 9 focuses on big molecule, 11 on small molecule (including PROTAC) and 6 on vaccines. Generally speaking, we found STAR SSE-listed biotech's to be earlier in stage than HKSE 18A biotech's. There are therefore higher levels of risk associated with STAR SSE-listed biotech's. In terms of quality, it is hard to tell since STAR SSE actively screen the applicants while HKSE relies on the market. At this point the best biotech's of China are primarily in HKSE and Nasdaq.

While so far STAR SSE hasn't become a source of excess liquidity for Chinese biotech's, it is on the border to become one.

Liquidity wise the two markets are similar, adjusting for the quality differences. Average 3M daily trading volume for STAR-SSE biotech's (ex-dual-listing) was Rmb26mn, while that for HKSE 18A biotech's (ex-dual-listing) is HK$35mn (Rmb31mn), according to our tabulation. This suggests the distortion of STAR SSE in biotech valuation hasn't become a major problem. But this can change, in our view, if STAR SSE admits more companies over a near future.

Having an exit, resale and restart mechanism is healthy

A healthy pharmaceutical ecosystem should consist of big pharma's, emerging biopharma's and biotech's. Big pharma's maintain a global salesforce and clinical network, supported by a sizable revenue and therefore must constantly scout out first-in-class (FIC) drugs globally to fill its sales pipeline. Emerging biopharma's have smaller sales and clinical footprints but are often first-class in particular therapeutic areas. They act as the price competitors to the big pharma's. Small biotech's are at the forefront of drug discovery and thus can be more focus on likely successes.

China's biotech ecosystem today lacks big pharma's but has a list of emerging biopharma's, which most are still one trick ponies trying to hit on the 2nd drug. We see state capital stepping in to support biotech innovation but complexity of drug development might lead to corruption and misuse of resources.

China's biotech ecosystem today lacks big pharma's who can pay top dollars but also few mid-sized pharma's who can spot winners. As such China must still rely on global pharma's and biopharmas to do the value discovery job. What China already has today is a list of emerging biopharma's which are characterized by (1) one or two in-house developed mini-blockbusters supporting a sales buildout, which (2) must use biosimilars and licensed-in's to fill the pipeline to support the salesforce, and (3) most still in severe cash outflow that must use periodic license-outs to recoup cashflow.

We can see in two of the above three mechanisms, involving the global biotech ecosystem is necessary. We see China's state capital stepping in to support early-stage biotech's in the place of big pharma's but complexity of drug development might lead to corruption and misuse of resources.

See the last page of the report for important disclosures

Oversea returnee scientists form the foundation of biotech start-ups

Among the 26 STAR SSE listed and filed biotech's (excl. dual listings), 14 were founded by oversea returnee scientists. Among the 35 HKSE 18A biotech's (excl. dual listings), 25 were founded by overseas returnee scientists. Further, the bigger the company, the high likelihood the founders are oversee returnee scientists. Within our innovative drug coverage of 7 companies, with the exception of JUNSHI, all are founded and owned by overseas returnee scientists. In fact JUNSHI was founded by a family of investment managers with an overseas returnee scientist, who subsequently left to found and own KeyMed, which was listed on HKSE in July 2021. JUNSHI's current CEO is again an oversea returnee scientist. Therefore, overseas returnee is vital to China's biotech scene.

Overseas returnees play a major role in founding Chinese biotech startups. The combination of experienced returnee scientists and abundant graduates forms the foundation of China's competitiveness.

The combination of experienced oversea returnee scientists and abundant supply of medical graduates form the human capital foundation of Chinese biotech's competitiveness. This could be put to risk if US starts to limit talent flow back to China.

US-China friction drags feet but is not as critical as semiconductor

With China's rise in global biotech value chain, it is inevitable that US has stepped up on its scrutinization. President Biden's <*National Biotechnology and Biomanufacturing Initiative*>, in our view, is aimed at evening the playing field with China in times of national emergency for undisrupted supply of essential drugs, API's, devices and components. At this time, we do not see China's advancement in biotechnology as posing a threat to the US leadership. But this day might come.

We believe Biden's initiative is a defensive measure as the US, at current stage, doesn't need to play unfairly.

We believe the likelihood of America's next step is to restrict the outflow of overseas returnee scientists to China. This, however, will be difficult to enforce, in our opinion, as US pharma's and biopharma's all sell drugs in China and therefore employ Chinese nationals. Further, as we examine the HKSE 18A and STAR SSE biotech's, we found most of the founders came from biotech, instead of major pharma, or even biopharma, backgrounds. Only after these companies become established did the Chinese executives from major pharma's and biopharma's join. This tells us that the founder's pool of Chinese biotech's is a risk-taking breed, which is very different from the semiconductors, in which, thanks to narrowing path of technology evolution, only employees from a handful of ever narrowing list of companies have relevant experience.

In semiconductor, only employees from an ever-narrowing list of companies have relevant experience in the cutting edge. In biotech this is not the case.

Geopolitical risk is mainly single country risk

From one end, innovative drug industry is more difficult to sanction because it doesn't involve a single point of "choke point" where US and its allies have an overwhelming dominance. But from the other end, the US market as the single biggest pharmaceutical market in the world (~40%), coupled with enormous product concentration risk of any drug company, means any innovative drug developer being denied the access to US market will instantly face a growth bottleneck. In our opinion, the US, EU and Japan forms a "common market" with frequently interacted regulatory activities in pharmaceuticals, perhaps more "common" than the semiconductor market. Therefore, it is important for Chinese innovative drug developers to stay neutral between governments.

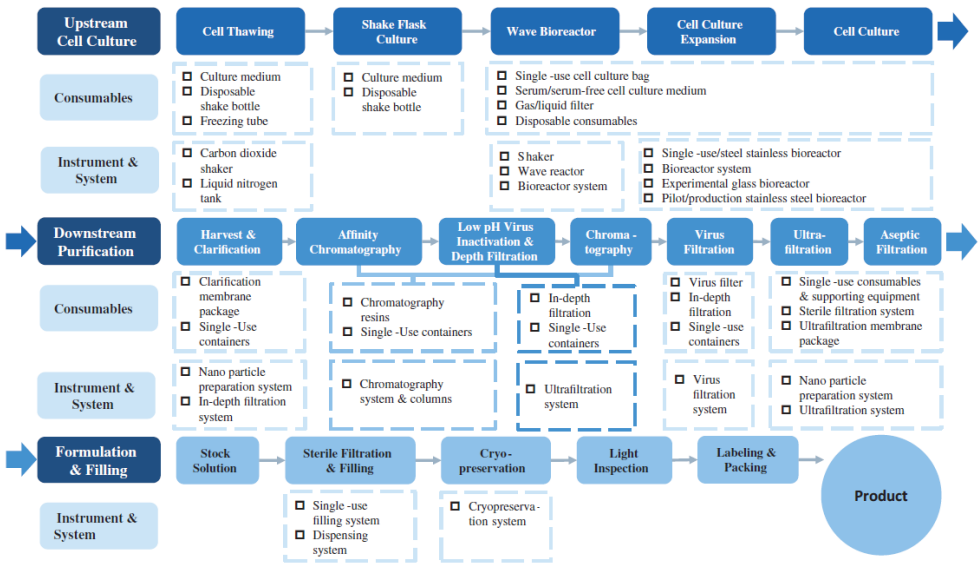
US, EU and Japan are three destination markets that together formed ~70% of global pharmaceutical end markets.

Supply chain restriction is relatively easy to overcome

From our understanding, although multinationals control most of the biologics manufacturing process market, supply chain is not a choke point for Chinese innovative drug developers. According to the prospectus of Shanghai Duoning Biotech (多宁生物), China's leading biologics process solution provider, biologics manufacturing mainly involves cell medium preparation, previous control of manufacturing environment, and subsequent filtering and testing of products. Global leaders include Thermo Fisher (TMO US, NR), Danaher (DHR US, NR), Sartorius AG (SRT GR, NR) and Tosoh (4042 JP, NR). Listco's in China include Tofflon (300171 CH, NR), Truking (300358 CH, NR). Startups in China include Lepure (乐纯生物) and JYSS (金仪盛世).

Biologics manufacturing involves transfer a gene encoding the desired protein into a "production cell.", multiplying it, and then harvest, filter and package it.

Exhibit 67. Biologics manufacturing process diagram



Source: Duoning Bio, Blue Lotus (2022/10/21)

In our view, a more pertinent risk is the low self-sufficiency ratio of scientific equipment used in biologics R&D and manufacturing. Today most of the High-Performance-Liquid-Chromatography (HPLC), Raman spectroscopy and Mass Spectroscopy equipment must be imported. However, the silver lining is that non-US vendors also can make these equipment, which most do not contain critical US technology or components, like semiconductor does.

Many scientific equipment can be imported from Europe or Japan.

See the last page of the report for important disclosures

Actively participating scientific communication helps

The US FDA is part of US Department of Health and Human Services (HHS) with an annual budget of US$6-8bn and a total headcount of 18K. Despite so, FDA's Centre for Drug Evaluation and Research (CDER) needs external help in evaluating drugs.

The academic leaders of ~300 is an important buffer between political clashes from China and US.

There are 12 advisory committees under CDER, among which two are the most related to drug approval: (1) Blood, Vaccine and Other Biologics; (2) Human Drugs Advisory Committee. There are a total of 21 advisory subcommittees, divided by therapeutic areas, with a total of ~300 advisors, mostly doctors and professors, serving under. FDA also has a Science Board of 14 members plus 8 vacancies. We believe these academic leaders form an important buffer between political forces that clashes from China and US. We believe the more Chinese innovative drug developers getting involved in global scientific communications, the less likely they get effectively sanctioned.

Military and diplomatic implication of biotech is a real concern

We believe FDA's advisories, the academic leaders of ~300, is an important buffer between political clashes that might result between US and China. But this is on a precondition that the subject matter doesn't involve military.

As the past pandemic of COVID-19 has shown, vaccines and drugs can be used as tools or weapons in diplomacy and military. At one end investors can be assured China's vested interest is to continue support innovative drug industry under the background of NDRL price cuts. At the other end a misinterpretation of weaponizing biotech can invite counter measures that tilt the industry to a tit-for-tat exercise.

To deal with that, development of innovative drug industry outside of the Western sphere becomes critical to the Chinese innovative drug industry, which will put it in a place to compete against generics and biosimilars. When our competitive pool gets enlarged to include generic and biosimilar producers worldwide, the matrix for evaluation also changes, which will further limit the number of leaders China can produce in innovative drugs.

There aren't many spots remain for a global innovative drug leader from China. The need to compete in generic and biosimilar further reduces that choice.

Valuation and peer analysis

In our view, the easy approval standards of CDE were partially responsible for the IPO boom and valuation premiums enjoyed by Chinese biotech's. Our study found a major reason behind Chinese clinical trial costs being substantially lower than global levels was trial design, i.e., single arm vs. randomized control. CDE's easy approval may not lead to ineffective drugs because the more stringent approval might be an overkill to begin with. But regardless, the tightening of innovative drug approval is going to be a global phenomenon and China will be no exception. This will result in a compression on stock valuations, in our view.

Easy approval may not lead to ineffective drug but tightening approval will certainly depress stock valuation.

Easier NDA approval from CDE led to higher valuation for biotech's

As aforementioned, CDE is now focusing on improving the regulatory mechanism to adhere to global standards. It has recently released documents calling for more stringent and standardized procedures for clinical trials. CDE has noticed the many homogeneous products are wastes of clinical resources and funds. With the continuous improvement of regulatory regime and track record, CDE/NMPA will gradually be recognized and accepted by other countries, and thereby facilitating Chinese innovative drug developers' push overseas. Before that, we believe the regulatory actions from CDE/NMPA will go through several rounds of tightening and relaxations.

Chinese biotech's are generally more expensive than global

Since most companies do not have earnings, price to sales is the only comparable matrix. Our picked universe of 11 Chinese Innovative drug Developers trade at 2023 P/S of 18x, bigger than Global Innovative Drug Developers 6.0, Chinese Generic Drug Developers' 5.6, Global Generic Drug Developers' 2.9 and Major Pharma's 4.9 (Exhibit 68).

Measured by PSG, Chinese Innovative Drug Developers aren't expensive. But the premise is sales growth must come with margin improvement down the road.

What Chinese innovative drug developers do offer is growth. Measured by PSG (Price to Sales divided by 3Yr. compounded sales growth rate), Chinese Innovative Drug Developers are traded at 0.28, below Global Innovative Drug Developers' 1.56, Chinese Generic Drug Developers' 0.33, above Global Generic Drug Developers' 0.26 but below Major Pharma's 0.90.

We believe the investment logic of Chinese Innovative Drug Developers is that their gross margin shall improve down the road with truly innovative drugs driving most of the future growth. If the growth actually comes from selling license-in, biosimilars or generic drugs, then the much lower multiples of the generic drug developers shall apply.

BGNE, RemeGen and Akeso are true innovative drug developers while ZLAB, Innovent and JUNSHI are either not or becoming not. We believe innovative drug developers' valuation premium must be derived from innovative drug development.

Exhibit 68. Peer comparison table

Sector		Price	Mkt Cap	PE (consensus)			PSG	PS (consensus)		EV/EBITDA (consensus)	
	Ticker	(Local)	(US$m)	2022E	2023E	2024E	2023E	2023E	2024E	2023E	2024E
Chinese innovative drug											
BeiGene Ltd	BGNE US	169.37	19,444	(11.9)	(16.0)	(22.0)	0.29	9.3	6.9	(11.9)	(16.6)
Zai Lab Ltd	ZLAB US	28.69	2,809	(5.7)	(6.3)	(9.9)	0.10	7.9	4.2	(3.3)	(4.8)
Legend Biotech Corp	LEGN US	47.63	7,816	(22.2)	(26.0)	(88)	0.58	37.4	19.9	(42.6)	141
I-Mab	IMAB US	3.88	322	(1.4)	(1.6)	(3.9)	0.06	5.0	3.1	8.0	10.0
Remegen Co Ltd	9995 HK	46.65	4,779	(38.5)	(64.3)	(202)	0.28	19.1	12.5	(60.4)	NM
Innovent Biologics Inc	1801 HK	30.2	5,886	(19.2)	(31.9)	(179)	0.20	6.2	4.8	(34.4)	NM
Shanghai Junshi Bio.	1877 HK	25.2	6,030	(24.0)	(55.8)	(427)	0.22	11.2	8.4	(77.1)	69
Akeso Inc	9926 HK	31.0	3,321	(23.8)	(36.9)	642	0.17	12.1	7.5	(34.7)	138
KeyMed Biosciences Inc	2162 HK	37.9	1,351	(20.6)	(15.3)	(17.4)	0.72	79.1	45.7	(11.5)	(12.6)
CARsgen Therapeutics	2171 HK	13.58	987	(16.2)	(12.4)	(13.9)	NM	123.0	22.3	(6.4)	(6.5)
InnoCare Pharma Ltd	9969 HK	9.51	2,275	(22.0)	(71.8)	(210)	NM	12.2	8.4	(38.4)	NM
Alphamab Oncology	9966 HK	6.18	739	(10.0)	(9.1)	(19.1)	0.11	13.6	5.1	(6.0)	(8.3)
Average			**55,761**	**(18.7)**	**(30.3)**	**(74)**	**0.28**	**17.9**	**10.3**	**(31.5)**	**29**
Global innovative drug											
Amgen Inc	AMGN US	251.94	134,770	14.5	13.9	12.9	1.54	5.0	4.8	10.9	10.5
Gilead Sciences Inc	GILD US	67.79	84,966	10.3	10.8	10.1	4.06	3.4	3.3	8.4	8.1
Seagen Inc	SGEN US	128.84	23,763	(37.1)	(100)	86.8	0.28	9.7	7.0	(195)	77.7
Vertex Pharmaceuticals	VRTX US	300	76,938	21.4	19.3	18.0	1.26	8.2	7.7	12.5	11.7
Regeneron	REGN US	713.91	77,822	16.5	15.8	14.7	1.23	6.2	5.8	10.8	10.1
Biogen Inc	BIIB US	267.615	38,834	16.1	17.1	17.5	NM	4.1	4.2	12.2	12.2
Alnylam Pharmaceuticals	ALNY US	198.88	23,871	(30.1)	(57.6)	112.6	0.32	14.7	9.8	(106)	61.3
BioMarin Pharmaceutical	BMRN US	90.01	16,695	50.8	22.7	14.1	0.25	6.1	4.9	21.8	10.8
Incyte Corp	INCY US	70.58	15,699	22.0	15.7	11.3	0.30	4.0	3.5	11.2	7.4
Average			**493,358**	**12.1**	**6.2**	**22.2**	**1.56**	**6.0**	**5.4**	**(4.4)**	**16**
Chinese generic drug											
Jiangsu Hengrui Medicine	600276 CH	39.97	35,262	58.2	50.4	42.0	0.53	9.6	8.3	41	36
Sino Biopharmaceutical	1177 HK	4.2	10,067	17.9	17.8	16.3	0.25	2.1	1.9	10.9	10.0
Shanghai Fosun Pharma.	2196 HK	19.6	10,853	2.5	1.9	1.7	NM	0.2	0.2	2	2
Genscript Biotech Corp	1548 HK	19.4	5,225	(18.5)	(28.9)	347.2	0.11	4.8	3.2	(6)	5.8
Kintor Pharmaceutical Ltd	9939 HK	12.6	654	(7.3)	302.5	18.5	NM	3.1	2.7	(18.3)	NM
CSPC Pharmaceutical	1093 HK	8.53	12,967	15.4	13.8	12.5	0.22	2.6	2.4	8.9	8.4
Average			**75,029**	**31.4**	**29.4**	**48.7**	**0.33**	**5.6**	**4.8**	**22**	**20**
Global generic drug											
Teva Pharmaceutical	TEVA US	8.44	9,373	3.3	3.3	3.1	0.39	0.6	0.6	6.3	6.1
Viatris Inc	VTRS US	9.38	11,374	2.7	2.8	2.9	NM	0.7	0.7	5.5	5.6
Sun Pharmaceutical	SUNP IN	977.7	28,389	28.5	24.2	21.7	0.37	4.9	4.4	17	15
Aurobindo Pharma Ltd	ARBP IN	524.45	3,719	11.8	9.7	9.6	0.09	1.1	1.0	5.6	5.1
Cipla Ltd/India	CIPLA IN	1134.75	11,083	29.3	23.6	21.0	0.30	3.5	3.2	15	13
Aspen Pharmacare	APN SJ	14854	3,656	10.6	9.6	8.7	NM	1.5	1.5	7.2	7.1
Dr Reddy's Laboratories	DRRD IN	4330.8	8,727	21.5	18.6	16.9	0.23	2.8	2.6	12	11
Hikma Pharmaceuticals	HIK LN	1197	2,968	7.3	6.5	6.3	0.19	1.1	1.0	5.4	5.3
Average			**79,288**	**18.8**	**16.0**	**14.5**	**0.26**	**2.9**	**2.6**	**11.8**	**11**
(TBC)											

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Sector		Price	Mkt Cap	PE (consensus)			PSG	PS (consensus)		EV/EBITDA (consensus)	
	Ticker	(Local)	(US$m)	2022E	2023E	2024E	2023E	2023E	2024E	2023E	2024E
Global major pharma											
AbbVie Inc	ABBV US	147.1	260,016	10.5	12.5	12.6	NM	4.7	4.7	11.4	11.3
AstraZeneca PLC	AZN LN	9720.0	169,589	16.5	14.7	12.3	0.53	3.6	3.4	11.9	9.9
Bristol-Myers Squibb Co	BMY US	72.2	154,187	9.5	9.1	9.0	1.12	3.3	3.2	7.9	7.7
Bayer AG	BAYN GY	50.0	48,330	6.4	6.4	5.8	0.76	1.0	1.0	6.5	6.2
GSK PLC	GSK Ln	1392.4	63,770	10.7	9.8	8.8	0.31	2.0	1.8	7.4	6.8
Horizon Therapeutics Plc	HZNP US	63.7	14,671	13.8	11.7	9.3	0.31	3.7	3.2	10.2	8.0
Johnson & Johnson	JNJ US	168.7	443,569	16.6	16.4	15.7	1.91	4.5	4.4	12.6	12.0
Eli Lilly & Co	LLY US	340.8	323,791	44.9	39.0	29.6	0.91	10.7	9.3	30.4	23.6
Merck & Co Inc	MRK US	95.7	242,359	13.0	13.2	11.4	1.27	4.2	4.0	10.6	9.5
Pfizer Inc	PFE US	45.0	252,275	6.9	8.7	10.4	NM	3.2	3.7	7.3	9.2
Roche Holding AG	ROG SW	324.4	270,104	16.1	15.9	14.5	1.17	4.2	4.0	11.6	10.7
Takeda Pharmaceutical	4502 JP	3719.0	39,966	7.3	8.0	8.1	NM	1.6	1.6	9.1	9.3
Daiichi Sankyo Co Ltd	4568 JP	4380.0	57,919	93.0	56.4	38.5	0.42	6.2	5.4	32.5	24.7
Average			**2,340,547**	**19.2**	**17.7**	**15.4**	**0.90**	**4.9**	**4.6**	**13.8**	**12.4**

Source: Bloomberg, Blue Lotus (2022/10/21). NM=Either no reliable data or facing revenue declines over the measurement period.

Appendix A: Acronyms

Exhibit 69. Acronyms

Acronym	Full name	Chinese name
ADC	Antibody Drug Conjugates	抗体偶联药物
ALK	Anaplastic lymphoma Kinase	间变性大细胞淋巴瘤
API	Active Pharmaceutical Ingredients	药物活性成分
Badan POM/BPOM	Badan Pengawas Obat dan Makanan	印度尼西亚食品与药物管理局
BCMA	B-cell Maturation Antigen	B 细胞成熟抗原
BDA	Biological Drug Applications	生物药物申请
BLA	Biologics License Application	生物许可申请
BsAb	Bispecific Antibody	双特异性抗体 (双抗)
BTKI	Bruton's Tyrosine Kinase	布鲁顿酪氨酸激酶抑制剂
CAR-T	Chimeric Antigen Receptor T-Cell Immunotherapy	嵌合抗原受体 T 细胞免疫疗法
CBRN	Chemical, Biological, Radiological and Nuclear	化学、 生物、 放射和核
CD19	Cluster of Differentiation 19	白细胞分化抗原
CDAC	Chimeric Degradation Activating Compound	蛋白降解
CDE	Center for Drug Evaluation (China)	中国药品审评中心
CDMO	Contract Development and Manufacturing Organization	定制研发生产机构
CDSCO	Central Drugs Standard Control Organization	中央药物标准控制组织（印度）
CLTA-4	Cytotoxic T-lymphocyte-associated Protein 4	细胞毒性 T 淋巴细胞相关蛋白 4
CMS	Centers for Medicare & Medicaid Services	联邦医疗保险和医疗补助服务中心
CRO	Contract Research Organization	委托研究机构
CXO	CRO、CMO、CDMO	医药外包
DOF	Diario Oficial de la Federacion	墨西哥政府公告
DRA	Drug Regulatory Authority of Pakistan	巴基斯坦药品监督管理局
EMA	European Medicines Agency	欧洲药品管理局
ESMO	European Society for Medical Oncology	欧洲肿瘤医学学会
FDA	Food and Drug Administration (USA)	美国食品药品监督管理局
FF	Fast Follower	快速追踪新药
FIC	First-In-Class	首创新药
GPC3	Glypican-3	磷脂酰肌醇蛋白聚糖 3
GPIF	Government Pension Investment Fund	日本政府养老金投资基金
HeFH	Heterozygous Familial Hypercholesterolemia	杂合子型家族性高胆固醇血症
HER-2	Human Epidermal Growth Factor Receptor 2	人表皮生长因子受体 2
HHS	Health and Human Services Department (USA)	美国卫生和福利部
IARC	International Agency for Research on Cancer	国际癌症研究机构
ICH	International Council for Harmonisation	国际人用药品注册技术协调会
IND	Investigative New Drug Application	新药申请
ITIM	Immunoreceptor Tyrosine-based Inhibitory Motif	免疫受体酪氨酸抑制基序
IVD	In Vitro Diagnosis	体外诊断
(TBC)		

Acronym	Full name	Chinese name
KRAS	Kirsten Rat Sarcoma Viral Oncogene	鼠类肉瘤病毒癌基因
LAG-3	Lymphocyte-activation Gene 3	淋巴细胞活化基因 3
mAb	Monoclonal Antibody	单克隆抗体 (单抗)
MOHFW	Ministry of Health and Family Welfare (India)	卫生和家庭福利部（印度）
MOHRSS	Ministry of Human Resources and Social Security	中国人力资源与社会保障部
MT	Me-too	跟随型创新
MTKI	Multitarget Tyrosine Kinase Inhibitor	多靶点酪氨酸酶抑制剂
NAFDAC	National Agency For Food and Drug Administration and Control	尼日利亚食品药品管控局
NBI	Nasdaq Biotechnology Index	纳斯达克生物指数
NCSES/NSF	National Center for Science and Engineering Statistics	国家科学与工程统计中心
NDA	New Drug Application	新药申请
NDRL	National Drug Reimbursement List	国家医保目录
NHSA	National Healthcare Security Administration	国家医疗保障局
NK	Natural Killer	自然杀手(细胞)
NMPA	National Medical Products Administration (China)	中国国家药品监督管理局
NPFA	National Pension Fund Association	日本国民年金基金联合会
NRA	National Regulatory Authorities	世界卫生组织备案国家监管机构
NSCLC	Non-small cell lung cancer	非小细胞肺癌
OR	Overall Survival	总生存时间
ORR	Overall Response Rate	总缓解率
OS	Overall Survival Rate	总生存率
PARP	Poly ADP-Ribose Polymerase	多聚 ADP 核醣聚合酶
PCSK9	Proprotein Convertase Subtilisin/Kexin Type 9	循环中前蛋白转化酶蛋白酶/kexin9 型
PD-1	Programmed Death-1	程序性死亡受体 1
PD-L1	Programmed Cell Death 1 Ligand 1	细胞程序性死亡-配体 1
PFS	Progression Free Survival	无进展生存时间
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)	日本医药品医疗器械综合机构
PROTAC	Proteolysis-Targeting Chimeras	蛋白水解靶向嵌合体
RCT	Randomized Control Test	随机对照实验
ROS1	ROS Proto-oncogene 1, Receptor Tyrosine Kinase	原癌基因酪氨酸激酶
SAT	Single-Arm-Test	单臂实验
SIMM of CAS	Shanghai Institute of Materia. Medica. of Chinese Academy of Science	中科院上海药物研究所
S-Protein	Spike Protein	棘突蛋白
SRA	Stringent Regulatory Authorities	世界卫生组织认定严格监管机构
SSA	Social Security Administration	美国社会保障总署
STAR	A-share Science and Technology Innovation Board	A 股科技创新委员会
TCM	Traditional Chinese Medicine	传统中医药
TCR-T	T-cell Receptor	T 细胞治疗
TIGIT (TBC)	T cell Ig and ITIM domain	T 细胞免疫球蛋白和 ITIM 结构域

Acronym	Full name	Chinese name
TKI	Tyrosine Kinase Inhibitor	酪氨酸激酶抑制剂
TRK	Tyrosine Kinase Receptor	酪氨酸激酶受体
USCES	US Current Employment Statistics	美国劳工统计局
VGEF	Vascular Endothelial Growth Factor	血管内皮生长因子

Source: Blue Lotus (2022/10/21)

Appendix B: Drug names

Exhibit 70. Drug names

Medical name	Trade name	R&D code	Chinese name	Developer	Marketer
Acalabrutinib	*Calquence*	-	阿卡替尼	AstraZeneca	AstraZeneca
Adagrasib	-	MRTX849	阿达格拉西布	Mirati	ZLAB
Adalimumab	*Humira biosimilar*	UBP1211	阿达木单抗	AbbVie	AbbVie
Aducanumab	*ADUHELM*	-	阿杜那单抗	Biogen	Biogen
Alirocumab	*Praluent*	-	阿利库单抗	Regeneron/Sanofi	Regeneron/Sanofi
Anlotinib	-	-	盐酸安罗替尼	SinoBio	SinoBio
Apatinib Mesylate	*艾坦*	-	甲磺酸阿帕替尼	HENGRUI	HENGRUI
Atezolzumab	*Tecentriq*	-	阿替利珠单抗	Roche	Roche
Atorvastatin	*Liptor*	-	阿伐他汀	Pfizer	Pfizer
Avelumab	*Bavencio*	-	阿维单抗	Merck	Merck
Bamlanivimab	-	LY-CoV555/JT001	-	JUNSHI	Eli Lilly
Bevacizumab	*BYVASDA (Avastin biosimilar)*	JS501	-	ETANA	Innovent
Baloxavir Marboxil	Xofluza	-	巴洛沙韦	Roche	Roche
Blinatumomab	*BLINCYTO*	-	博纳吐单抗	Amgen	Amgen
Brentuximab Vedotin	*Adcetris*	-	维布西妥单抗	Seagen	Seagen
Cadonilimab	*开坦尼*	AK104	卡度尼利单抗	Akeso	Akeso
Camrelizumab	*艾瑞卡*	-	卡瑞利珠单抗	HENGRUI	HENGRUI
Cemiplimab	*Libtayo*	-	西米普利单抗	Regeneron/Sanofi	Regeneron
Ciltacabtagene Autoleucel	*CARVYKTI*	-	西达基奥仑赛	Legend Bio	Johnson & Johnson
CT041	-	CT041	-	CARsgen	CARsgen
CT053	-	CT053	-	CARsgen	CARsgen
Disitamab Vedotin	*爱地西*	RC48	维迪西妥单抗	RemeGen	Seagen
Dostarlimab	*Jemperli*	-	多塔利单抗	GSK	GSK
Durvalumab	*Imfinzi*	-	德瓦鲁单抗	AstraZeneca	AstraZeneca
Emicizumab	*Hemlibra*	-	艾美赛珠单抗	Roche	Roche
Envafolimab	*恩维达*	KN035	恩沃利单抗	Alphamab	Alphamab
Etesevimab	*Hemlibra*	JS016/LY-CoV016	埃特司韦单抗	JUNSHI	Eli Lilly
Evolocumab	*Repatha*	-	依洛尤单抗	Amgen	Amgen
Ezetimibe	*Ezetrol*	-	依折麦布	Merck	Merck
Fluzoparib	-	SHR3162	氟唑帕利	HENGRUI	HENGRUI
Geptanolimab	*杰诺*	GB226	杰洛利单抗	GENOR	GENOR
IBI326	-	IBI326/CT103A	-	ISAO	Innovent
Ibrutinib	*Imbruvica*	-	依鲁替尼	AbbVie/J&J	AbbVie/J&J
Ivonescimab	-	AK102	依沃西单抗	Akeso	Akeso
Niraparib	*ZEJULA*	MK-4827	尼拉帕尼	GSK	GSK/ZLAB
Nivolumab	*OPDIVO*	-	纳武单抗	BMS	BMS
Ociperlimab	-	BGB-A1207	欧司珀利单抗	BeiGene	Novartis
(TBC)					

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Medical name	Trade name	R&D code	Chinese name	Developer	Marketer
Olaparib	*Lynparza*	-	奥拉帕尼	AstraZeneca	AstraZeneca
Ongericimab	-	JS002	昂戈瑞西单抗	JUNSHI	JUNSHI
Pemigatinib	*Pemazyre*	-	培米替尼	Incyte	Innovent
Pembrolizumab	*KEYTRUDA*	-	帕博利珠單抗	Merck	Merck
Penpulimab	*安尼可*	AK105	派安普利单抗	Akeso	SinoBio
Pucotenlimab	*普佑恒*	HX008	普特利单抗	LEPU	LEPU
Pyrotinib	*艾瑞妮*	-	马来酸吡咯替尼	HENGRUI	HENGRUI
Ramucirumab	*Cyramza*	-	雷莫芦单抗	Eli Lilly	Innovent
Rituximab	*HALPRYZA (Rituximab Biosimilar)*	-	利妥昔单抗	Eli Lilly	Innovent
Telitacicept	*泰爱*	RC18	泰它西普	RemeGen	RemeGen
RC28	-	RC28	RC28	RemeGen	RemeGen
Repotrectinib	-	TPX0005	瑞波替尼	BMS	ZLAB
Selpercatinib	*Retevmo*	-	赛哌替尼	Eli Lilly	Innovent
Senaparib	-	IMP4297/JS109	-	Impact	JUNSHI
Serplulimab	*汉斯狄*	HLX10	斯鲁利单抗	Henlius	Henlius
Sintilimab	*TYVVT*	IBI308	信迪利单抗	Innovent	Innovent/Eli Lilly
Sitravatinib	-	MGCD516	-	Mirati	BeiGene
Sotorasib	*LUMYKRAS*	AMG510	索托拉西布	Amgen	BeiGene
Sugemalimab	*Cejemly*	CS1001	舒格利单抗	Cstone	Pfizer
Tafolecimab	-	IBI 306	托莱西单抗	Innovent	Innovent
Tebotelimab	-	MGD 013	特泊利单抗	MacroGenics	ZLAB
Tislelizumab	*百泽安*	BGB-A317	替雷利珠单抗	BeiGene	Novartis
Tisotumab Vedotin-tftv	*Tivdak*	-	替索单抗	Seagen	Seagen/ZLAB
Toripalimab	*妥益*	JS001	特瑞普利单抗	JUNSHI	JUNSHI
Trastruzumab Deruxtecan	*Enhertu*	DS-8201	德喜曲妥珠单抗	Daiichi Sankyo	AstraZeneca
Trastuzumab Emtansine	*KADCYLA*	-	恩美曲妥珠单抗	Roche	Roche
Zanidatamab	-	ZM25	泽尼达妥单抗	Zymeworks	BeiGene
Zanubrutinib	*BRUKINSA*	BGB-3111	泽布替尼	BeiGene	BeiGene
Zimberelimab	*誉妥*	AB122	赛帕利单抗	Gloria/Arcus	Gloria

Source: Blue Lotus (2022/10/21)

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