



# China's future bellwethers

**A profile of the generation that will write China's next chapter:  
BioCentury's Scene Setter analysis for the 2021 China Healthcare Conference**

**(Chinese version immediately follows English presentation)**

# What are the stories that will write China's Next Chapter?

China's footprint in the global biopharma landscape has been forged by its first bellwethers, companies such as BeiGene Ltd., Zai Lab Ltd. and Innovent Biologics Inc. These pioneers upended the topography of me-too and service companies by planting the flag for innovative drug development. Those stalwarts, founded since 2010, now boast market caps over \$10 billion and a record of delivering multiple products to patients.

That elite group of innovators is likely to grow, as several biotechs now are on the verge of gaining revenues from recently or soon-to-be approved products.

Behind them lies a host of companies in the story-telling phase that will shape the China biotech ecosystem over the next decade and determine what and how big a role China plays in global drug development.

BioCentury's Scene Setter for the 8th BioCentury-BayHelix China Healthcare Summit analyzes the cohort of biotechs from which new bellwethers in therapeutics will likely emerge: the 47 companies that have raised more than \$100 million in private funding or an IPO since the start of 2020, before having any marketed products.

Examining the profiles of these companies through the lens of innovation, the analysis asks: What are the stories that will write the Next Chapter for China?

# China's Risk and Innovation Profile

The 2021 BioCentury China Scene Setter finds that the second generation of bellwethers has fluency in their parent class's mother tongue – creating drugs for unmet needs. But they also are writing a new language of risk-taking and cutting-edge science that will compete with the top biotechs worldwide.

However, China's chance to lead is not uniform. It excels in diseases such as cancer and technologies such as next-generation antibodies. It is gaining ground in areas such as autoimmune disease and cell therapies. But bets in orphan diseases and gene therapies are only starting to penetrate the could-be bellwethers, and China has few high-fliers in areas such as T cell engagers or targeted protein degradation that are hot topics in the West.

# Key Findings

- 1) **China's emerging leaders in therapeutics are focused on creating sustainable businesses.** Platform companies are now more common, and draw more funding, than pipeline companies that use in-licensing to build their first portfolio. But both strategies are yielding future leaders with deep pipelines of clinical candidates. Single-asset companies, a model that has been popular in Europe, are not a feature among this group.
- 2) **Almost all the bellwether class are gearing for the next generation of innovation.** They boast first-in-class targets, new modalities or next-generation technologies. By these measures, the public companies are taking greater target and technology risk than the private ones, though the latter are more likely to stake their lead program on a ground-breaking product.
- 3) **International investors are growing their stake in China's future leaders.** While China is backing its own talent, both public and private companies are drawing increasing interest from around the world. Investors are looking for differentiation beyond cancer and PD-1s, with areas such as ophthalmology and infectious disease growing in momentum.

# Analysis details

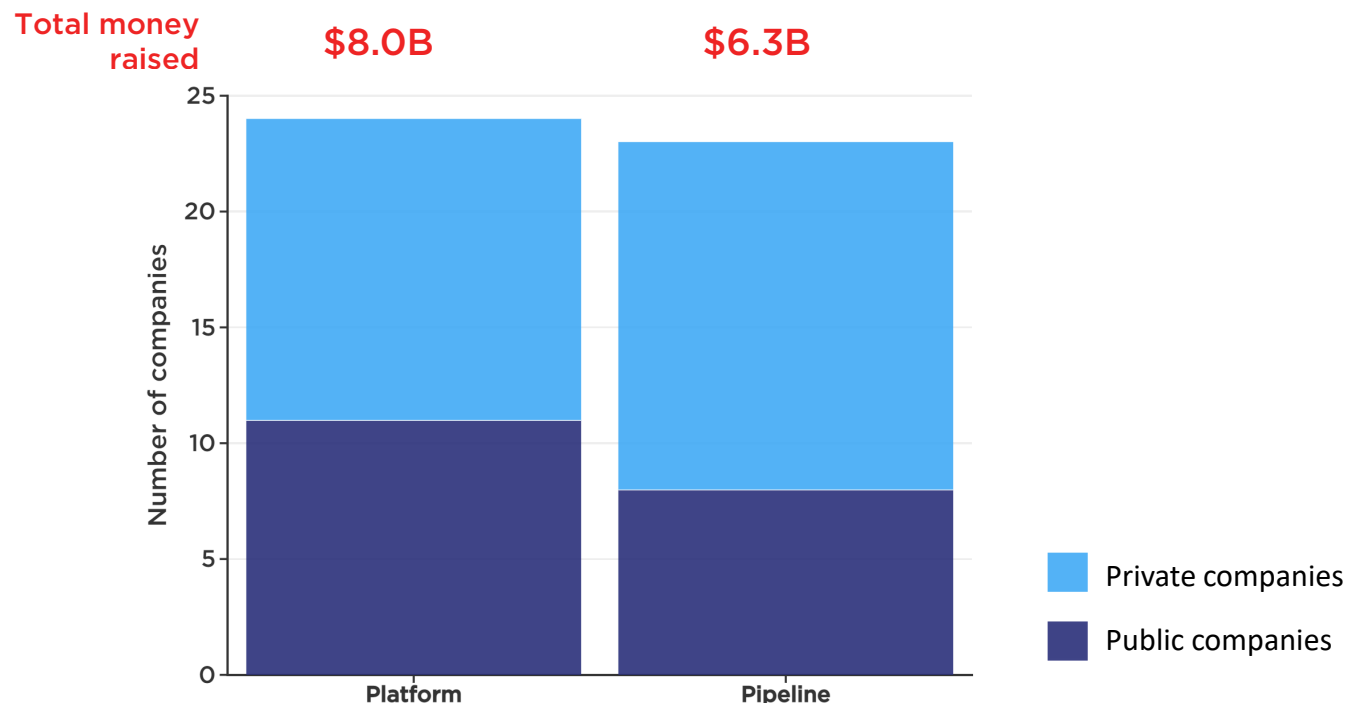
- ❑ Potential 2nd-generation bellwethers\* include:
  - ❑ Private companies that raised  $\geq$  \$100M in venture financing since Jan 2020
  - ❑ Public companies that raised  $\geq$  \$100M in an IPO since Jan 2020
  - ❑ Companies that are developing therapeutics or vaccines
- ❑ The analysis excludes:
  - ❑ Companies with marketed therapeutics at the time of financing
  - ❑ Companies that provide only provide services and do not have their own pipelines
- ❑ Definitions:
  - ❑ **Pipeline** companies contain a series of assets but not a unifying technology
  - ❑ **Platform** companies have a technology that yields multiple assets
  - ❑ **First in class** is defined for any clinical program that addresses:
    - ❑ A target where no drugs is approved in the same disease OR
    - ❑ An established target using a new modality

\* These companies can be found in BioCentury's BCIQ database. The analysis was based on information through Sept. 30, 2021

# China's next bellwethers are planning for the long term

Buying or building, they're creating portfolios for sustainable businesses

Company strategy for China's bellwether class

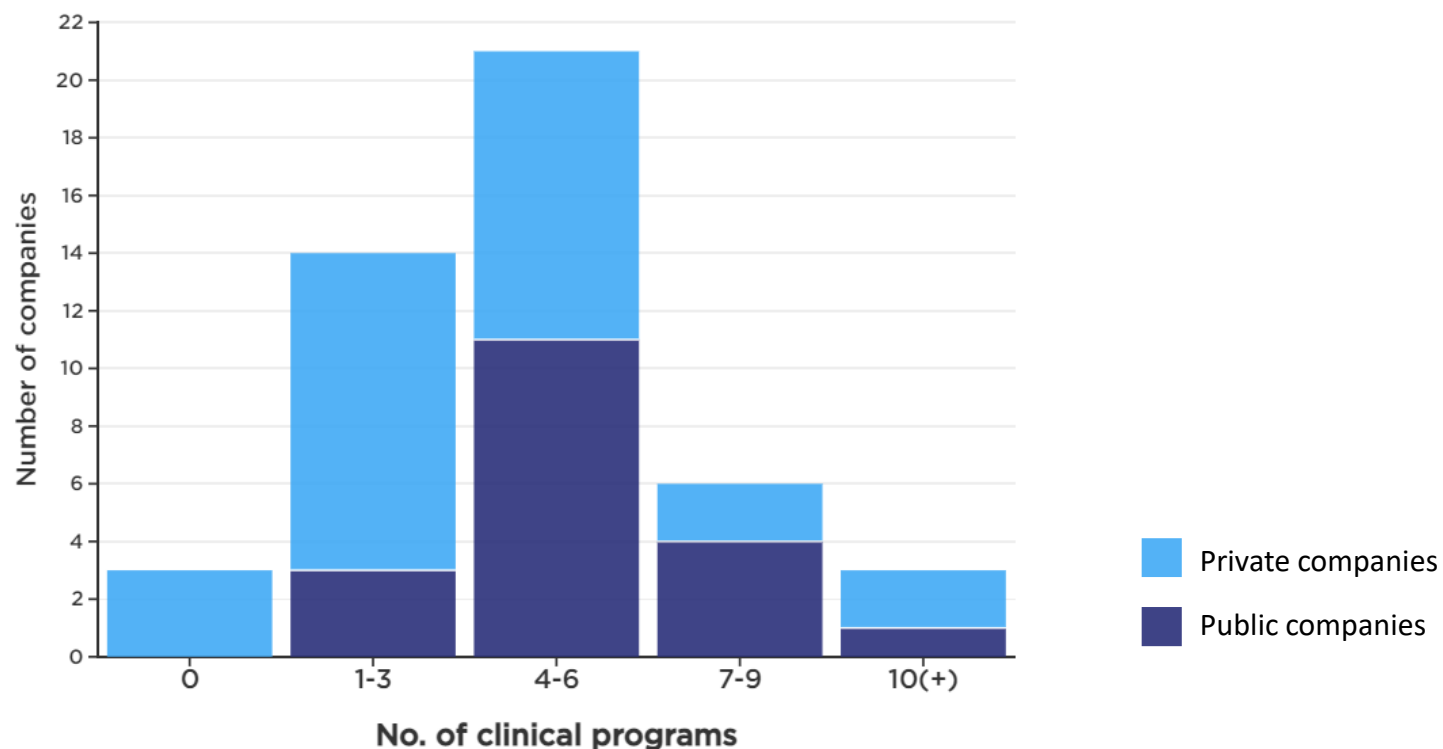


- ❑ The next bellwethers are equally likely to have programs born elsewhere (pipeline companies) as to have invented in house (platform companies)
  - ❑ 17 of 23 pipeline companies have in-licensed assets from ex-China biopharmas
- ❑ Investors are more enthusiastic about platform than pipeline strategies; single-asset companies aren't in the mix
  - ❑ Platform companies have raised 27% more in aggregate since founding than pipeline companies

# And they have deep clinical pipelines

The majority have at least four clinical programs

**Pipeline size for China's bellwether class**

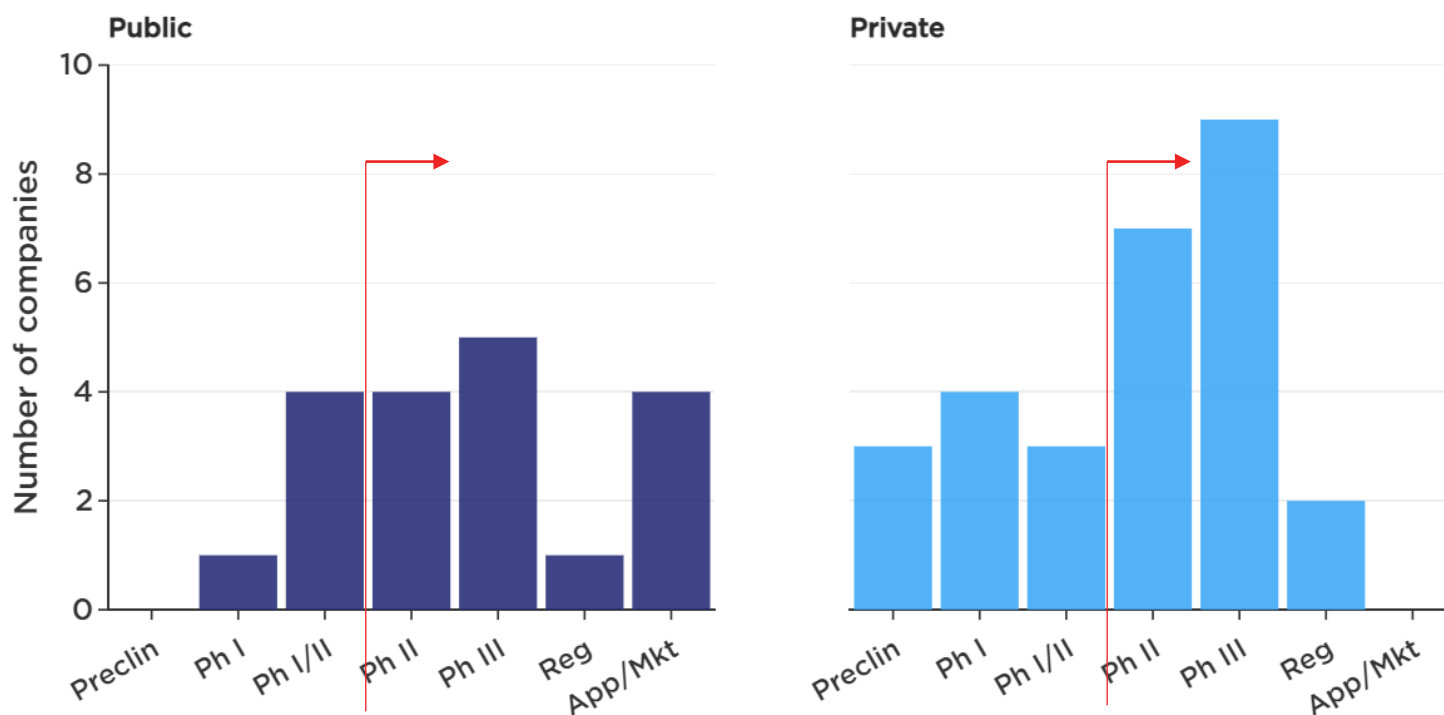


- ❑ Public companies that could reach bellwether class have rich pipelines — well beyond the HKEX Chapter 18A minimum requirement of one clinical program that's finished Phase I
- ❑ Almost all the leading private companies are in the clinic, in some cases with 10 or more programs

# The next bellwethers will make their mark soon

More than 20 companies have lead assets in pivotal trials or registration

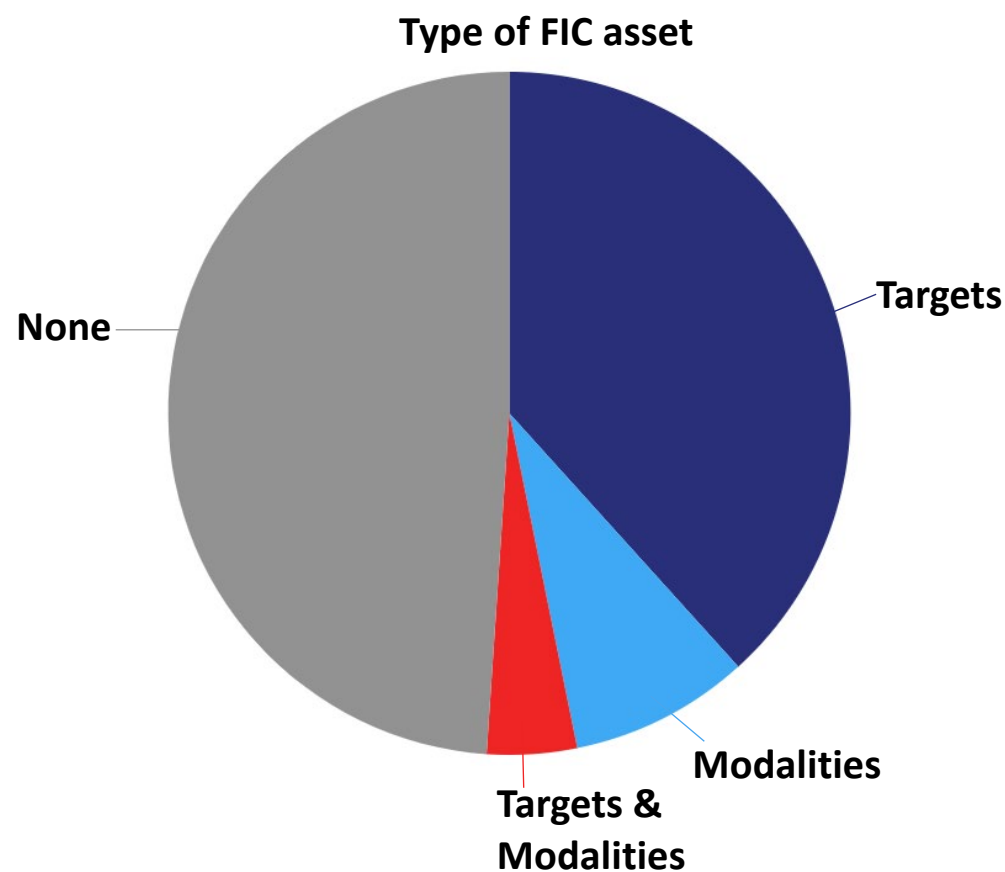
Phase of lead products



- ❑ Most lead programs in Phase II or later are made in China: 31% are in-licensed from foreign companies
- ❑ Four public companies have had a product approved since their IPO

# Future leaders are flush with first-in-class programs . . .

Half of the group (24/47) have potential FIC assets

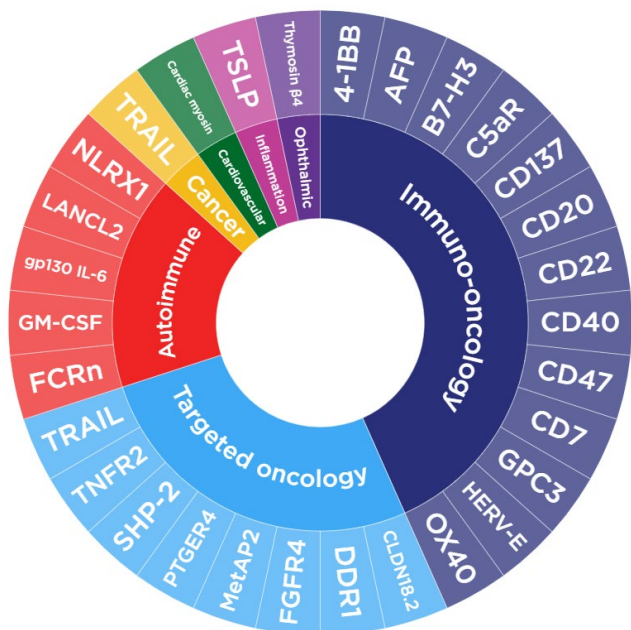


- ❑ FIC programs fit two molds:
  - ❑ **18** companies are pursuing novel targets where no products are approved
  - ❑ **4** companies are using new modalities against established targets
  - ❑ **2** companies are pursuing both models
- ❑ The PD-1 game has moved on:
  - ❑ Only 10% (5/47) have a conventional anti-PD-1 or PD-L1 mAb in the pipeline
  - ❑ 5 companies have a bispecific targeting PD-1/PD-L1 in clinical development; 3 have preclinical programs
  - ❑ 1 company has a cytokine-conjugated PD-1 construct

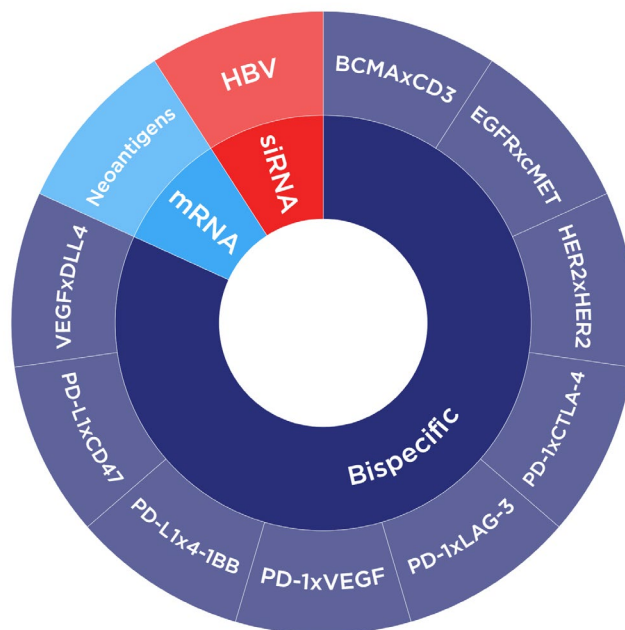
# First-in-class potential covers broad ground

With little clustering around individual targets, future bellwethers could deliver a wide impact

**FIC targets:**  
No approved products



**FIC programs:**  
New modalities, established targets

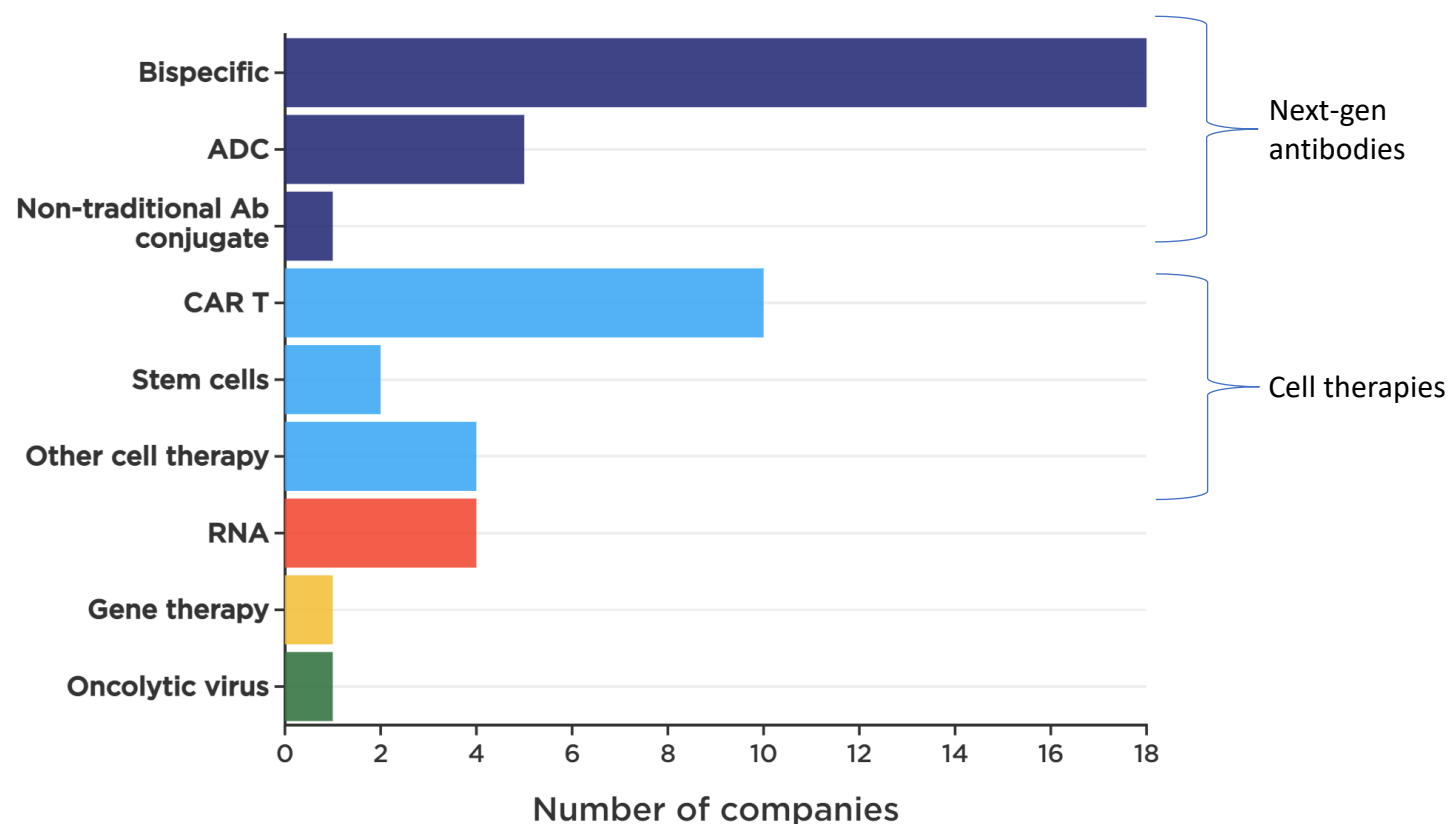


- ❑ Bispecifics companies are not flocking to traditional T cell engagers
- ❑ But several are coupling established targets in new ways, or creating dual-checkpoint inhibitors to overcome resistance
  - ❑ 4 have bispecifics targeting CD3; 2 are combining CD3 with a potential FIC target
  - ❑ 15 are focused on other bispecific structures that cover 8 FIC targets
- ❑ Four companies are targeting CLDN18.2, a major player in gastric cancers highly prevalent in China
- ❑ No other targets are in more than two companies' pipelines

# ... And new modalities are now the norm

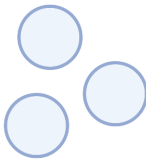

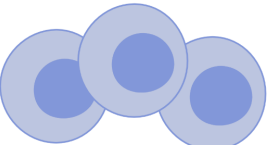












Two-thirds of the future leaders class have new modalities in their pipeline

Companies with new modalities in their pipelines



- ❑ Next-gen antibody formats lead – a traditional stronghold in China – but cell therapies are a growing focus
  - ❑ Strength is in T cell therapies for cancer
  - ❑ Little activity in NK cells, and no disclosed programs in NKT, myeloid or other immune cell therapies
- ❑ DNA/RNA based therapies are only starting to feature among the leaders

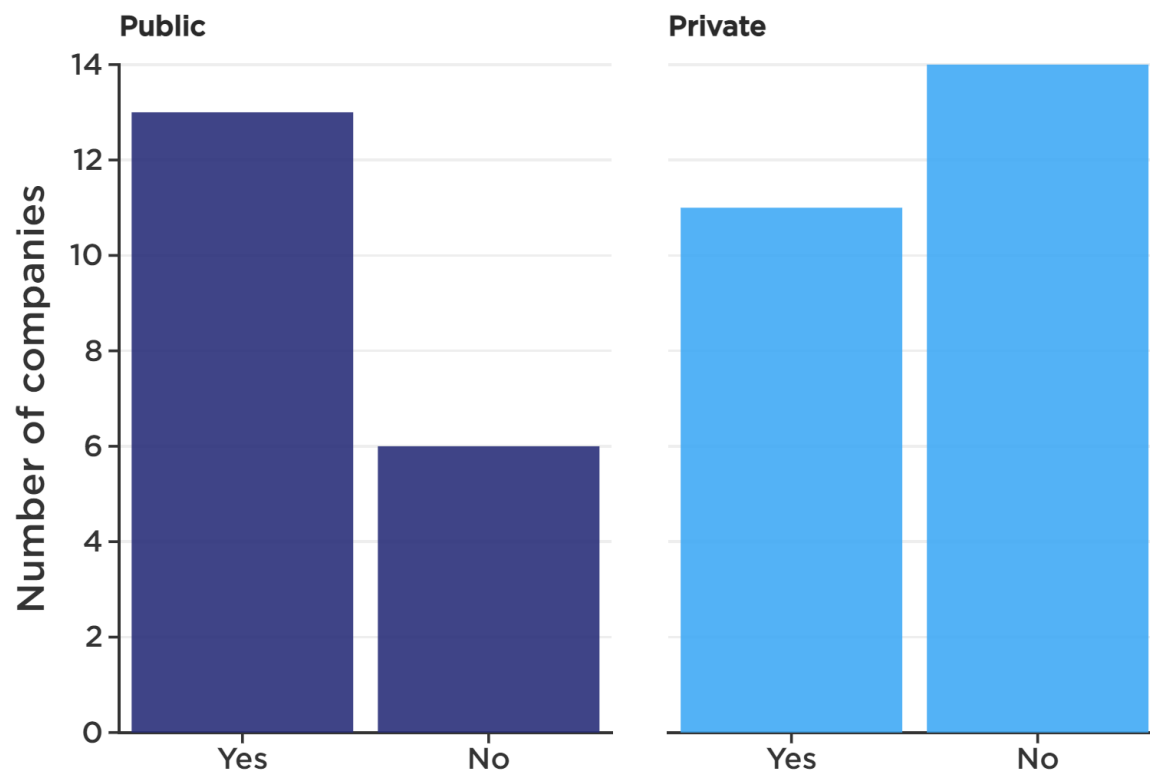
# Future leaders building at the forefront of validated modalities

 Small molecule	 Antibodies	 Cell therapy	 Gene therapy
 PROTAC (1)   Allosteric inhibitor (1)	 Bispecific ADC (1)   Antibody-cytokine conjugate (2)   Heavy chain only bispecific (1)   Conditionally active mAb, bispecific, ADC (1)	 Dual CAR T (2)   Allogeneic CAR T (4)   Cytokine loaded CAR T/TCR (2)   NK cells (1)	 RNA base editing (1)

- ❑ Even as cell and gene therapies reach validation, with their first products on the market, China's bellwether class is building better versions, adding innovative edges to create next-generation new modalities
- ❑ Likewise, novel approaches to antibodies and small molecules – which have decades of validation – put this class in position to deliver first-in-class products

# Risk-taking differs across public and private groups

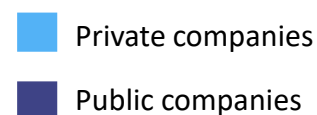
## First-in-class programs



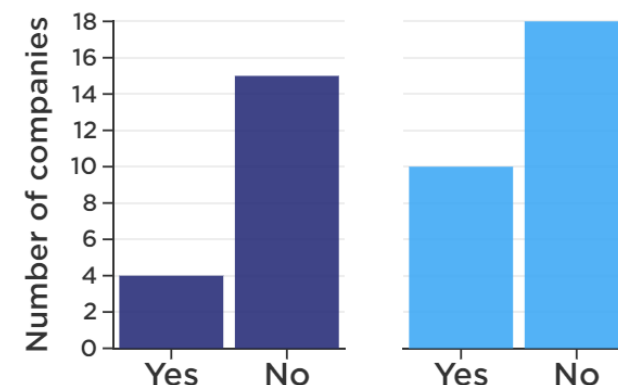
- ❑ Public companies in the future leaders class are more likely to have FIC assets in their pipeline, suggesting greater appetite for target risk. But deeper pipelines allow them to hedge with safer programs
  - ❑ Only 2 of 13 public companies have FIC assets as the lead program
- ❑ By contrast, in all 11 cases where a private company has a FIC program, the asset is a lead program

# Many future leaders betting the company on a new modality

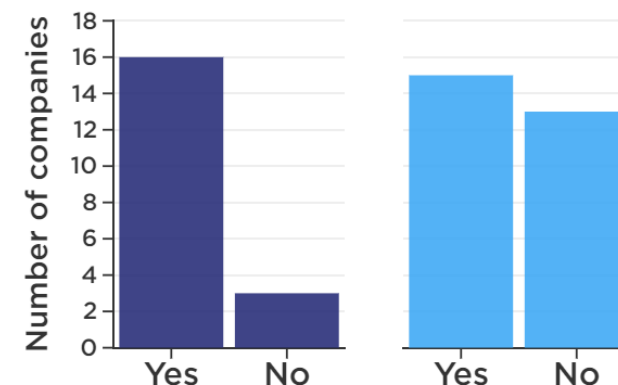
- ❑ Private companies are more likely to have a new modality in their **lead** program and are more likely to be pursuing a diverse set of modalities
- ❑ Four public companies have a T cell lead program; private companies are split between T cells, mRNA, stem cells and bispecifics, with bispecifics accounting for the most lead programs (4)
- ❑ Public companies may not be depending on new modalities, but almost all (84%) are fostering new modality programs compared with just over half (54%) for private companies



### Lead program is new modality

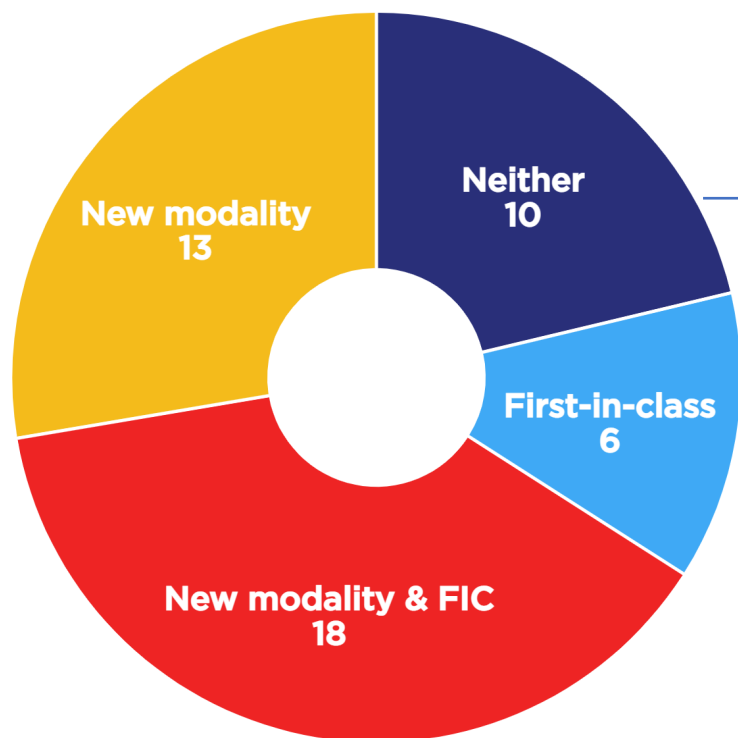


### New modality in pipeline



# Companies find alternative ways to shine

Companies lacking FIC and new modalities offer other value propositions to draw funding

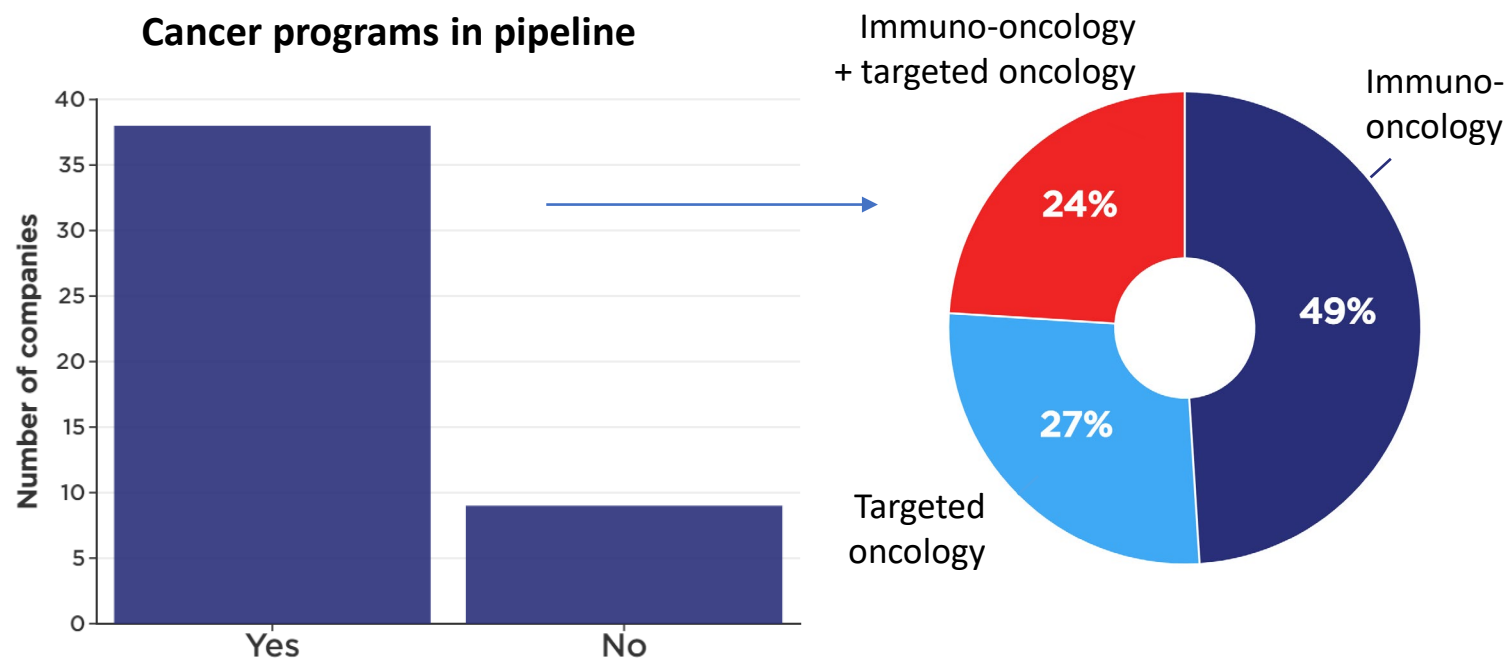


Strategies of companies without new modalities or FIC programs

Strategy	
Best-in-class	2
Fast follower	2
Innovative traditional modality platform	1
New preclinical targets	1
Delivery formulation	1
Undisclosed	3

# Is a presence in oncology still a must-have?

80% have at least one cancer program; 71% of those are in immuno-oncology

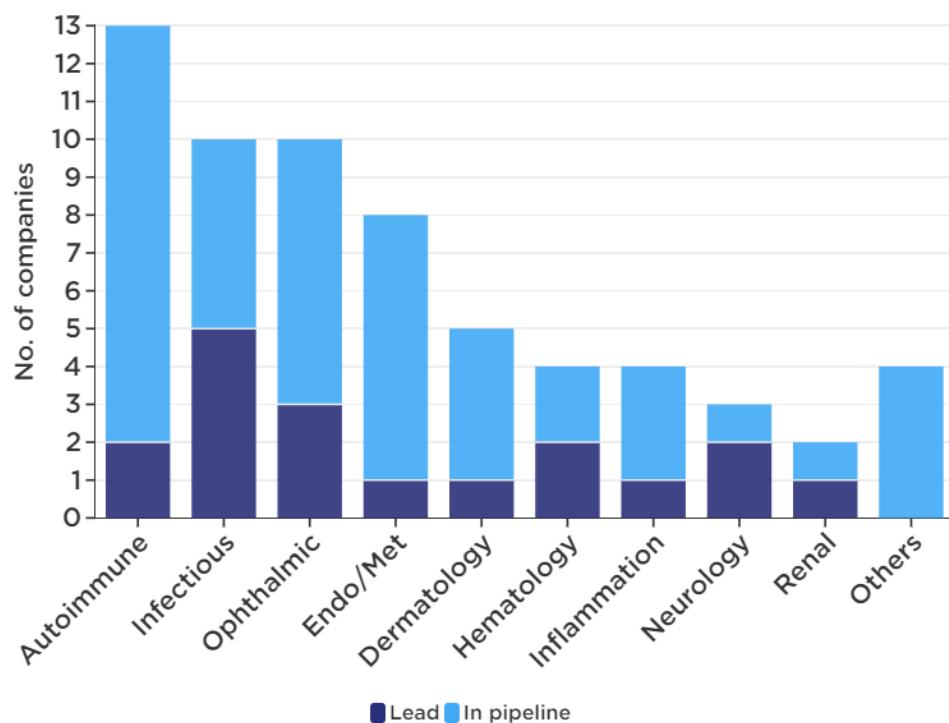


- ❑ China's government welcomes a crowded cancer space – it can drive down prices in NRDL tendering negotiations
- ❑ But are investors starting to look for differentiation? 20% of the potential bellwhethers *don't* have a cancer program

# China-prevalent diseases will dictate the agenda

As cancer gets crowded, newer biotechs branch into more areas to attract investment

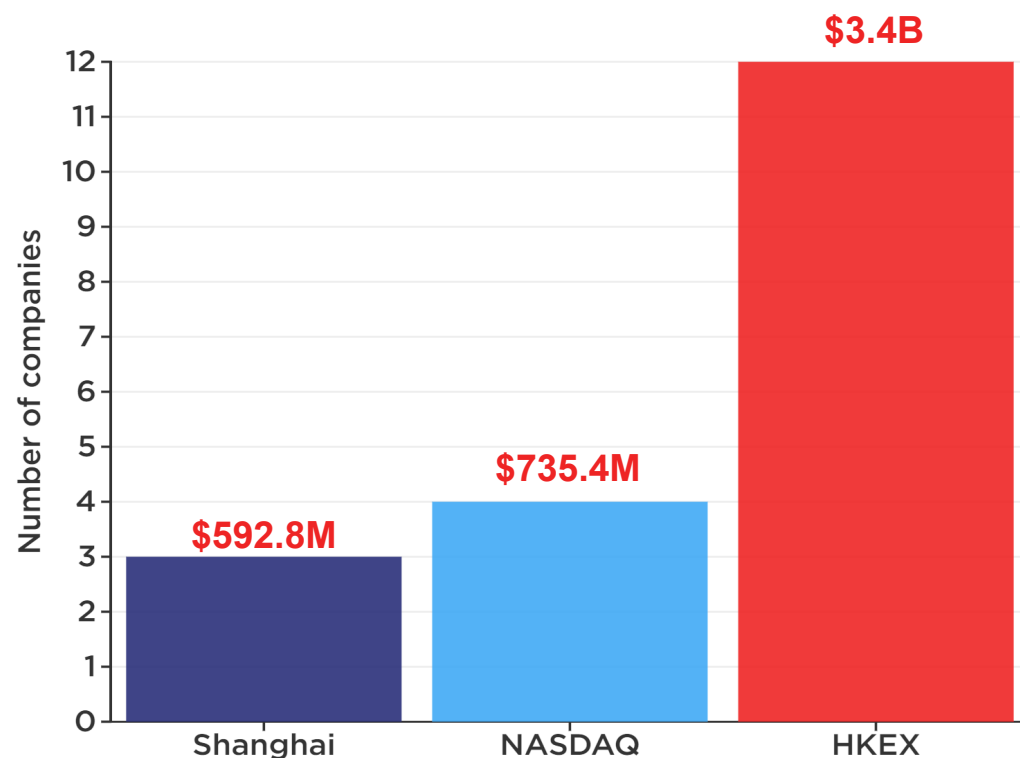
Non-cancer disease areas in company pipelines



- ❑ Chinese infectious disease plays looking well beyond COVID
  - ❑ 5 of the 10 infectious disease companies are in COVID; 4 of those 5 also have other infectious programs
  - ❑ Bacterial infections, EBV, Flu, TB, HIV, Rabies, RSV feature in the leadership class programs
- ❑ Ophthalmic disease has jumped to the front, an area to watch
- ❑ Autoimmunity and diabetes needs in China could put endocrine/metabolic companies in play with the same, heavily invested, areas in the West
- ❑ But neurology is not yet seeing the rebirth of enthusiasm taking place in the U.S.

# Future leaders find global investors on local exchanges

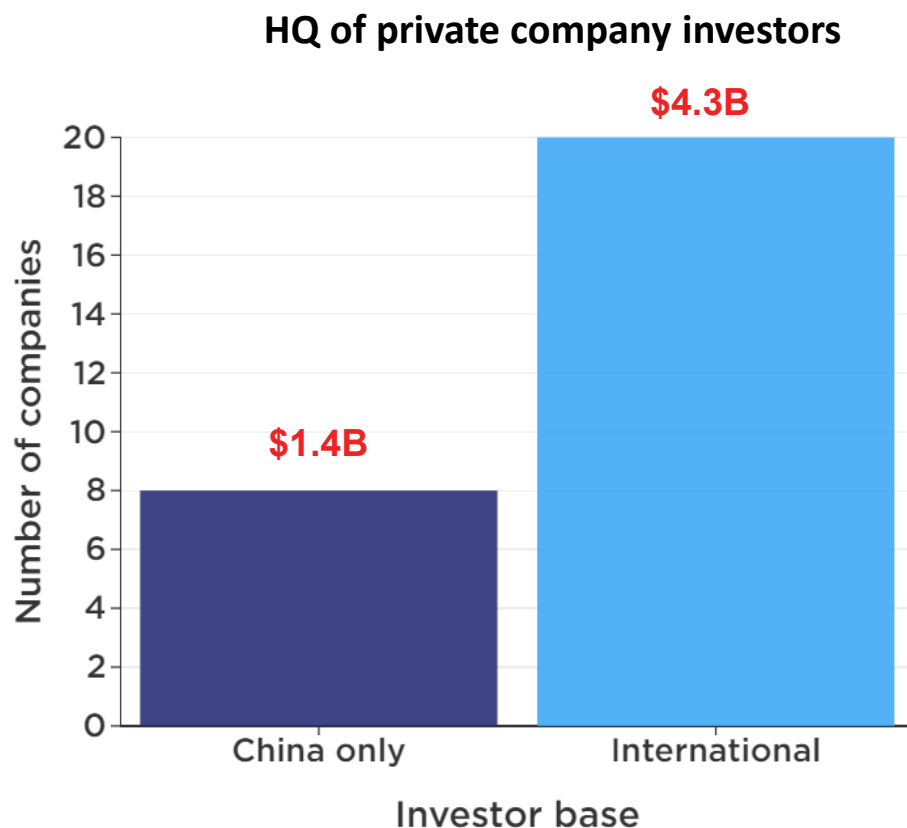
IPO exchanges for the public bellwether group



- ❑ More companies are choosing to list in Hong Kong, which is proving a good route
  - ❑ Average IPO of future bellwethers on HKEX was \$283.4M
  - ❑ Average IPO of future bellwethers on NASDAQ was \$183.9M
- ❑ Dual listings by the parent class of bellwethers are becoming more common. It remains to be seen whether the next-gen class will seek the same advantages
  - ❑ Access to different investor base
  - ❑ Hedge against geopolitical challenges of NASDAQ-only listing

# The broadening appeal of China's innovation

The vast majority of the private bellwether candidates have international investors



- ❑ 71% of the future leaders were backed by international investors
  - ❑ Less than one quarter of the money raised for private companies is from China syndicates only
- ❑ At least 30 different investors outside of Asia are backing Chinese newcos
  - ❑ 3 are headquartered in Singapore
- ❑ Investors in private companies include VCs, hedge funds, sovereign wealth funds, other biopharmas, private equity and global asset management firms

## Thank You for Joining Us at The 8th BioCentury-BayHelix China Healthcare Summit!

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# China's future bellwethers

书写中国新篇章的一代企业概况：

BioCentury 对 2021 中国医疗保健峰会的场景设制分析

# What are the stories that will write China's Next Chapter?

在百济神州、再鼎医药和信达生物这些企业的带领下，中国正稳步迈入全球生物制药领域。这些先锋企业一改过往仿制药和服务类公司形象，立志要在创新药物研发领域大显身手。这几家中坚医药公司成立于 2010 年，目前市值均超过了 100 亿美元，且都拥有丰富的医疗产品。

随着一些生物技术在最近或者即将被批准上市的产品上实现商业化应用，越来越多的企业可能会加入这一优秀的改革大军。

在他们背后，还有一大批公司正处于企划阶段，这些公司将在未来十年构建中国生物技术生态系统，并确定中国在全球药物研发中的职责与巨大作用。

BioCentury 在第 8 届 BioCentury-BayHelix 中国医疗峰会上的场景设制分析中指出，这些技术很可能会催生出新的医疗领军企业：自 2020 年初以来，有 47 家公司在没有任何产品上市以前，私募基金或首次公开募股 (IPO) 的规模超过 1 亿美元。

通过创新视角审视这些公司的概况，该分析报告提出：将书写中国新篇章的这些故事到底是什么？

# China's Risk and Innovation Profile

2021 年 BioCentury 中国场景设制分析 发现，第二代领军企业很好地继承了上一代企业按需制药的传统。不过，他们在风险承担和尖端科学方面有着独到之处，有实力与世界顶尖生物技术公司一较高下。

然而，中国领先世界的机会并不统一。中国擅长癌症等疾病的治疗和新一代抗体等技术的研发。在自身免疫性疾病和细胞疗法领域，中国越来越有话语权。但中国未来的领军企业才刚刚开始接触罕见病治疗手段和基因疗法知识，且中国在 T 细胞衔接器或靶向蛋白降解技术等西方热门话题领域，鲜有顶尖人才。

## Key Findings

- 1) **中国异军突起的医疗领军企业聚焦于创造可持续的商业模式。**如今，平台公司遍地开花，相比那些依靠许可引进建立第一个投资组合的产品线公司，他们能够募集更多资金。但这两种策略都在催生出拥有临床候选药深度产品线的未来领军企业。风靡欧洲的单资产型公司并不在内。
- 2) **几乎所有的领军企业都在为新一代创新技术做准备。**他们有着首创具有新靶点的药、全新用药模式或者新一代技术。尽管私营企业将自己的重点项目押注在突破性产品上的可能性更大，但通过这些手段，上市企业要比私营企业承担更多的目标和技术风险。
- 3) **国际投资者正在加大对中国未来领军企业的投资力度。**尽管中国一直在扶持国内的企业，但上市公司和私营企业也吸引了越来越多的国外投资者。随着诸如眼科、传染病防治等领域越来越热门，投资者们正在寻找癌症和 PD-1 以外的差异化产品。

# Analysis details

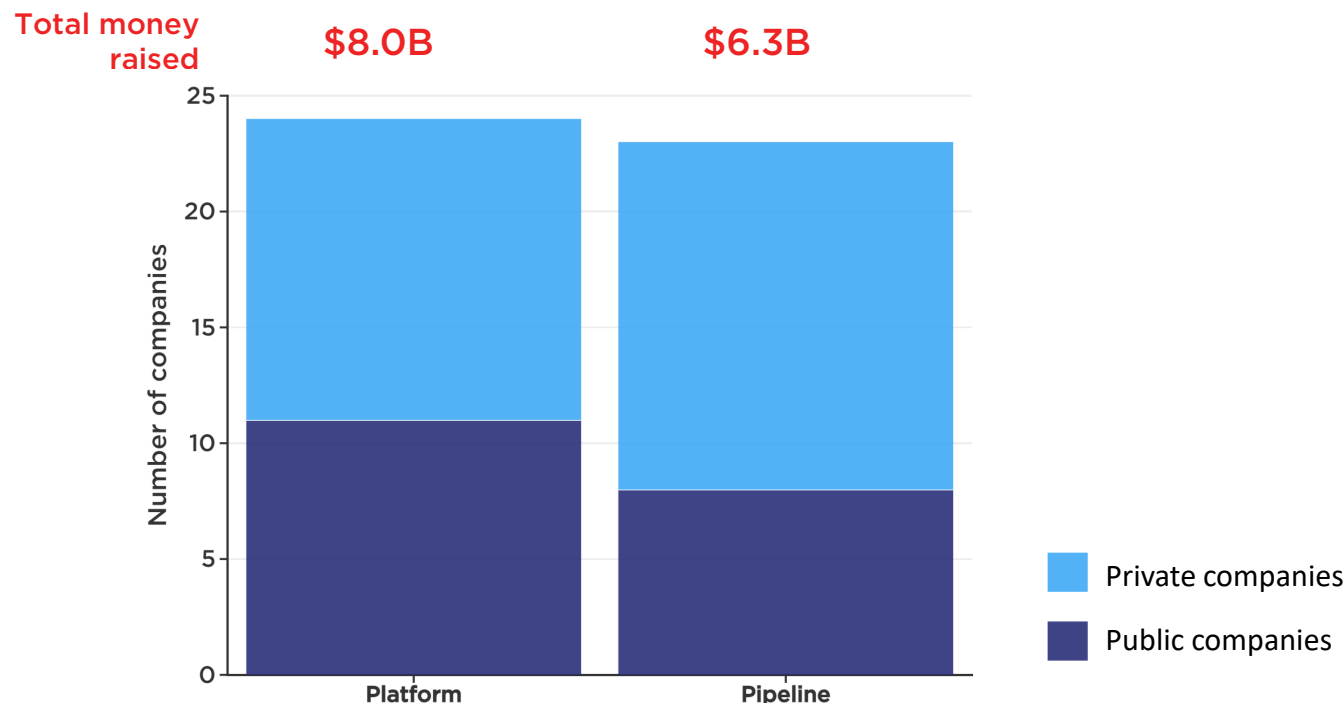
- ❑ 有机会成为第二代领军企业\*的条件包括：
  - ❑ 自 2020 年 1 月以来，风险融资大于或等于 1 亿美元的私营企业
  - ❑ 自 2020 年 1 月以来，IPO大于或等于 1 亿美元的上市公司
  - ❑ 正在研发治疗方案或疫苗的企业
- ❑ 分析报告将以下企业排除在外：
  - ❑ 融资时已有商业化治疗方案的企业
  - ❑ 只提供服务，而没有自己研发产品线的企业
- ❑ 定义：
  - ❑ 产品线公司拥有一系列资产，但没有统一的技术
  - ❑ 平台公司拥有创造多种资产的技术
  - ❑ 首创新药是指符合以下条件的临床项目：
    - ❑ 同种疾病中没有已经获批的具有该新靶点的药物
    - ❑ 或者采用全新用药方式研发已知靶点的药物

\* These companies can be found in BioCentury's BCIQ database. The analysis was based on information through Sept. 30, 2021

# China's next bellwethers are planning for the long term

不管是通过收购还是自创，他们都在推出资产组合使商业发展有可持续性

Company strategy for China's bellwether class

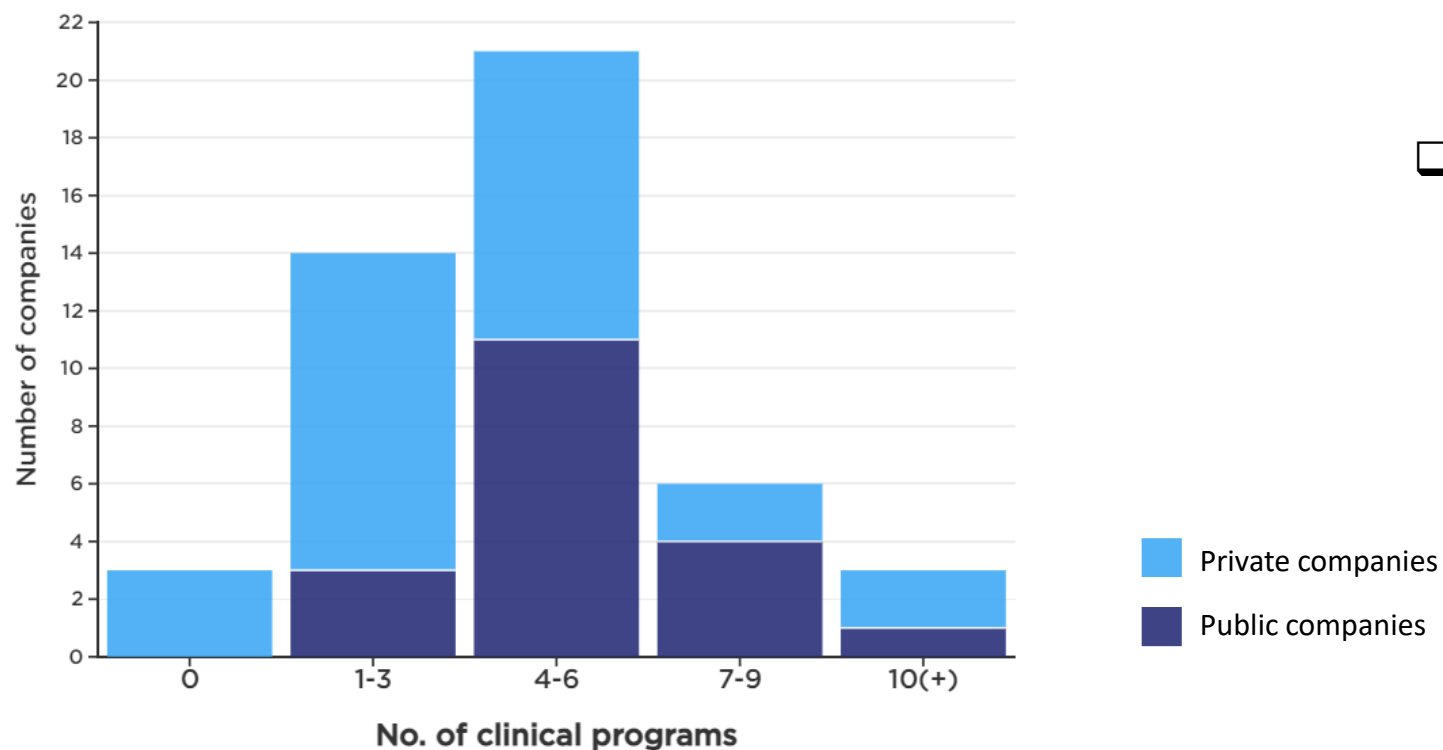


- ❑ 下一批领军企业同样有可能在其他地方孵化项目（产品线公司），也有可能是在内部孵化（平台公司）
  - ❑ 23 家产品线公司中，有 17 家拥有境外生物制药公司的引入许可资产
- ❑ 相比产品线策略，投资者更青睐平台策略；单资产型公司不在该范畴
  - ❑ 自成立以来，平台公司累计融资要比产品线公司多出 27%

# And they have deep clinical pipelines

大部分公司拥有至少4 个临床项目

Pipeline size for China's bellwether class

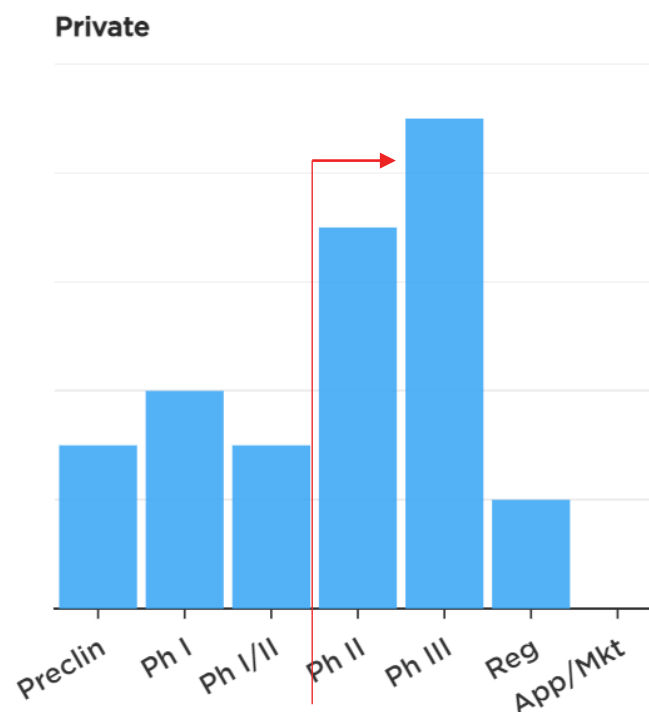
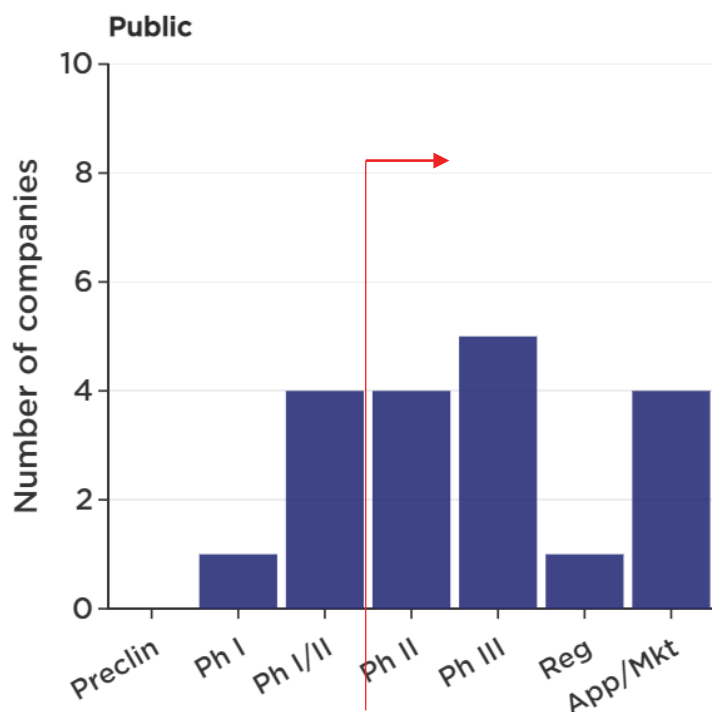


- 有机会成为领军企业的上市公司都有丰富的产品线，远远超出港交所第 18A 章对一个已完成 I 期的临床项目的最低要求
- 几乎所有领先的私营企业都有临床项目，有些甚至多于10个

# The next bellwethers will make their mark soon

超过 20 家公司在关键性试验或注册中拥有主导资产

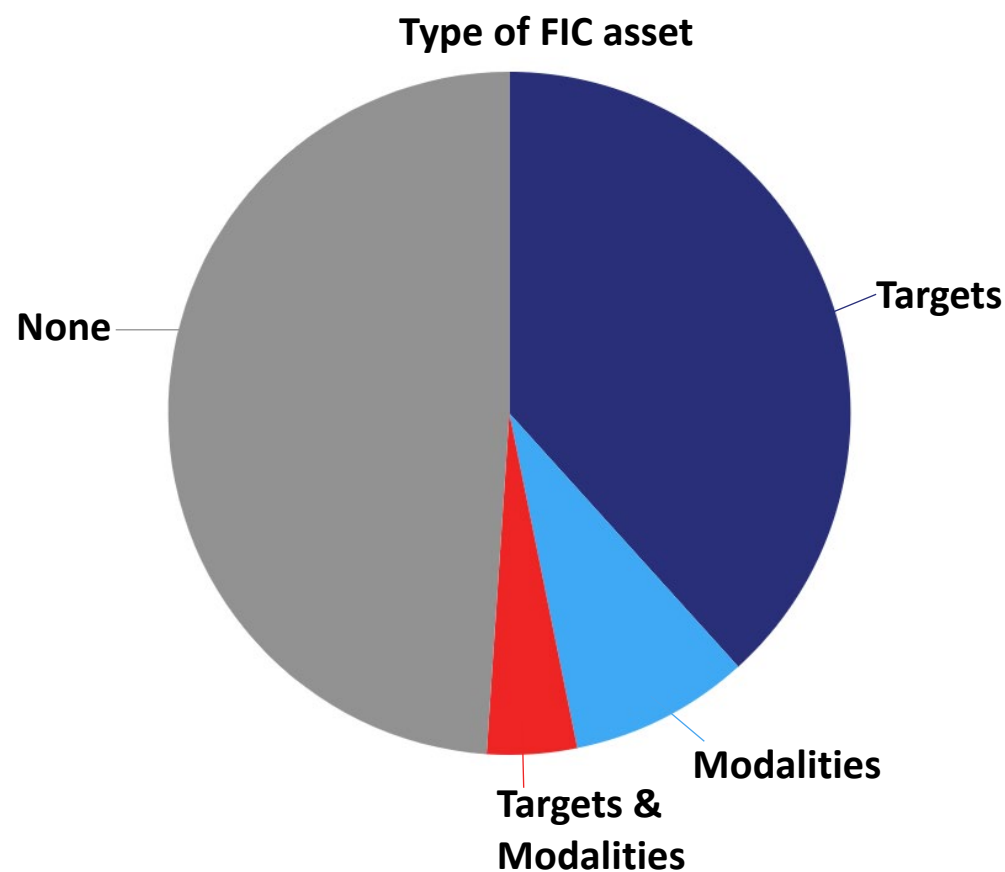
Phase of lead products



- 大部分 II 期及以后的主导项目都在中国开展：其中有 31% 是通过引入境外公司许可方式
- 自发行 IPO 以来，有 4 家上市公司已拥有获批产品

# Future leaders are flush with first-in-class programs . . .

半数公司 (24/47) 拥有潜在 FIC 资产



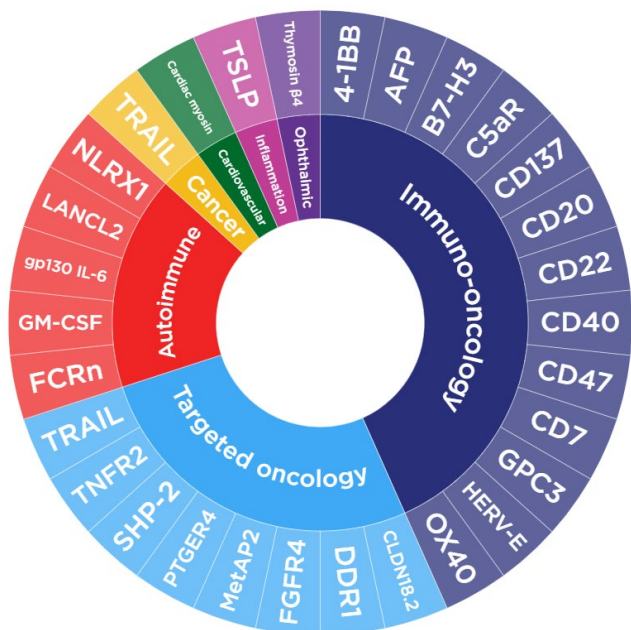
- FIC 项目有两种模式：
  - 18 家公司正在研发未获批的新型靶点
  - 4 家公司正在采用全新用药模式研发已知靶点的药物
  - 2 家公司采用了上述两种模式
- PD-1 竞赛愈演愈烈：
  - 只有 10% (5/47) 的公司产品线拥有传统的 PD-1 抑制剂或 PD-L1 mAb
  - 5 家公司有针对 PD-1/PD-L1 的双特异性药物处于临床研发阶段；3 家公司拥有临床前期项目
  - 1 家公司拥有共轭细胞因子 PD-1 构造技术

# First-in-class potential covers broad ground

未来的领军企业不会围绕相同的药物靶点，因此将带来更为广泛的影响

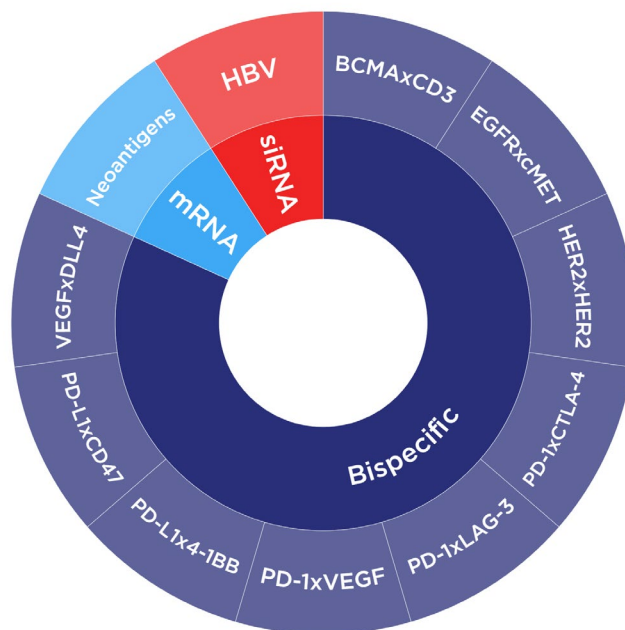
## FIC targets:

No approved products



## FIC programs:

New modalities, established targets

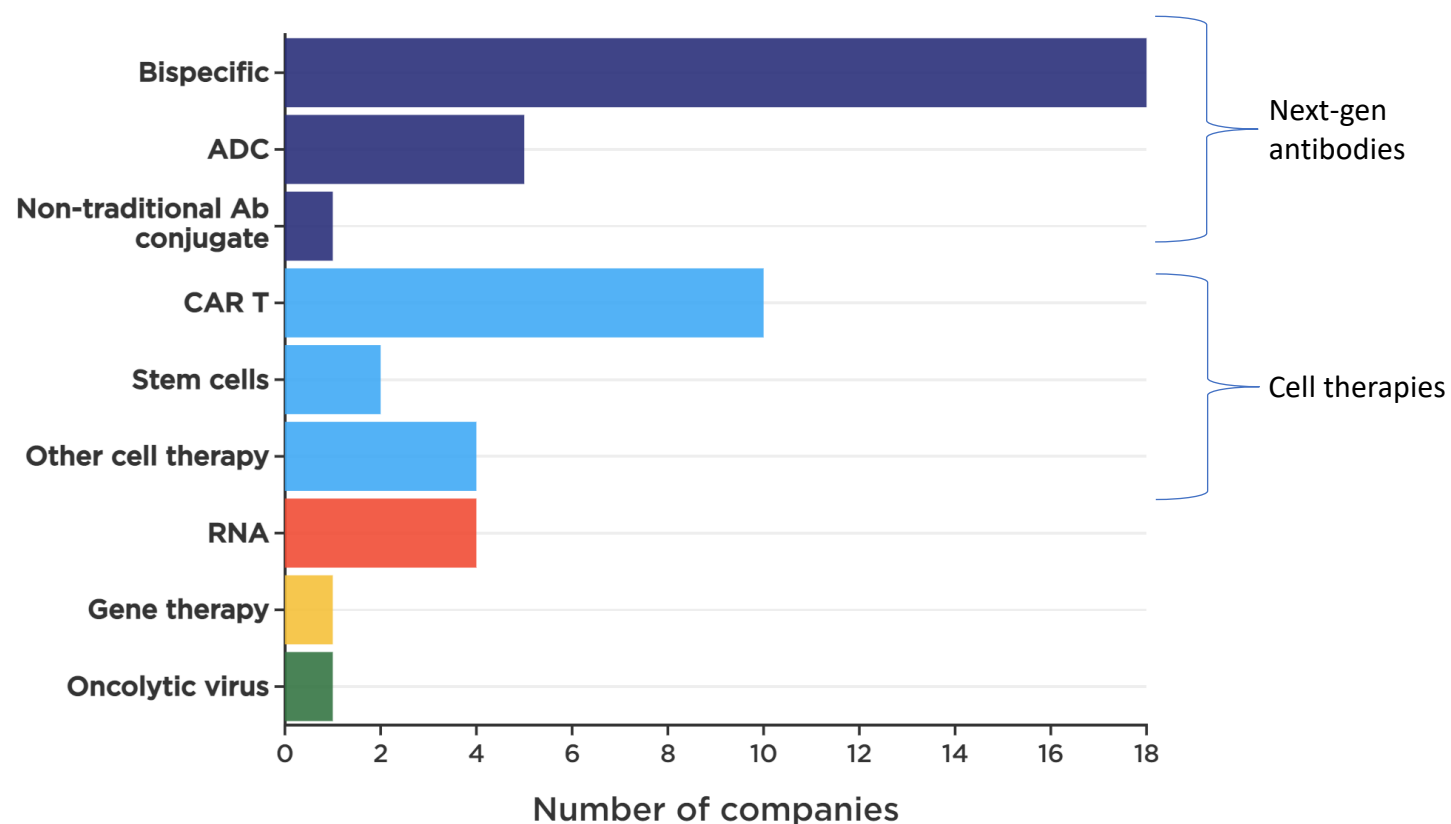


- ❑ 双特异性药企未集中转向传统的 T 细胞衔接器
- ❑ 但有几家公司正在以新的方式将现有靶点结合起来，或创造双检查点抑制剂以克服抗性
  - ❑ 4 家公司拥有针对 CD3 的双特异性药物；2 家公司将 CD3 与潜在 FIC 药物靶点相结合
  - ❑ 15 家公司专注于涵盖 8 种 FIC 药物靶点的其他双特异性药物构造技术
- ❑ 4 家公司专注于 CLDN18.2 靶点研究，该靶点在中国高发的胃癌中起重要作用
- ❑ 没有其他靶点被超过两家公司产品线研发

# ... And new modalities are now the norm

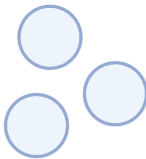

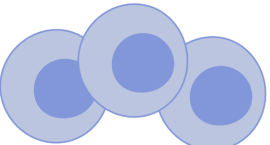







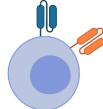

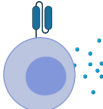


2/3 的未来领军企业产品线拥有全新用药模式

Companies with new modalities in their pipelines



- 新一代抗体形式占主导地位，其中中国依旧是传统据点，但细胞疗法正得到越来越多的关注
  - 医疗力量集中于癌症的 T 细胞疗法
  - 在 NK 细胞方面的项目很少，在 NKT、骨髓或其他免疫细胞治疗方面无公开项目
- 这些领军企业刚开始采用 DNA/RNA 疗法

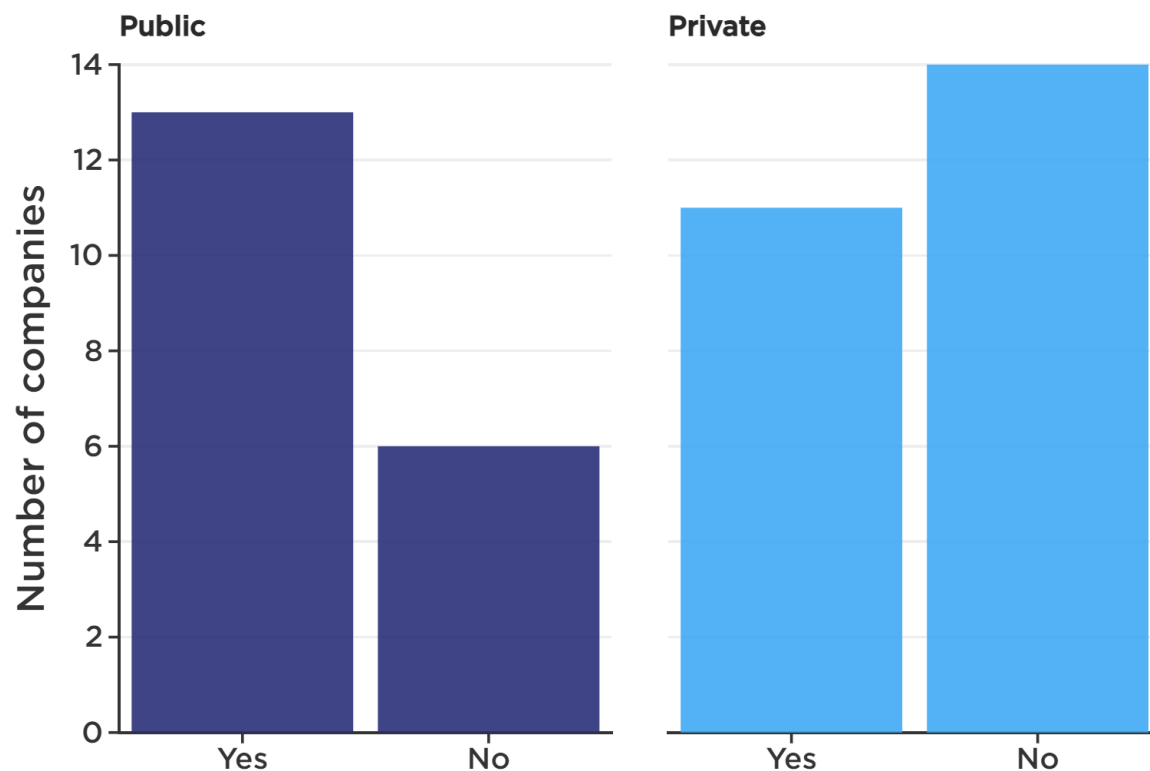
# Future leaders building at the forefront of validated modalities

 Small molecule	 Antibodies	 Cell therapy	 Gene therapy
 PROTAC (1)   Allosteric inhibitor (1)	 Bispecific ADC (1)   Antibody-cytokine conjugate (2)   Heavy chain only bispecific (1)   Conditionally active mAb, bispecific, ADC (1)	 Dual CAR T (2)   Allogeneic CAR T (4)   Cytokine loaded CAR T/TCR (2)   NK cells (1)	 RNA base editing (1)

- 尽管细胞和基因疗法已经得到验证，第一款产品也已上市，但中国的领军企业正在打造改良版本，利用创新优势创造新一代全新用药模式
- 同样，对经过几十年验证的抗体和小分子疗法的创新，保证该类药物可以成为首创产品

# Risk-taking differs across public and private groups

## First-in-class programs



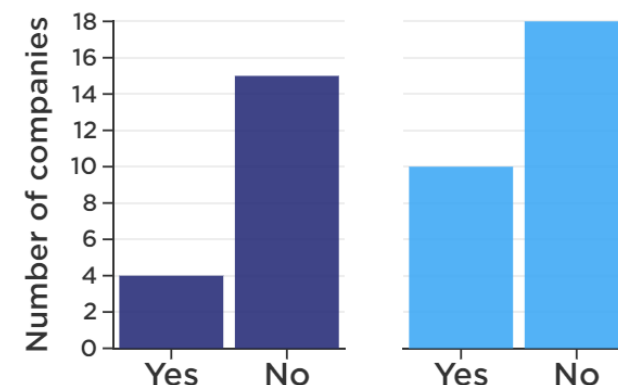
- ❑ 未来领军企业里的上市公司很可能会将 FIC 资产引入他们的产品线，这意味着他们对风险更大的靶点有更大的胃口。但更深度的产品线允许他们利用更安全的项目对冲风险
  - ❑ 13 家上市公司里只有 2 家公司将 FIC 资产作为主导项目
- ❑ 作为对比，另外 11 家拥有 FIC 项目的私营企业都将该资产作为主导项目

# Many future leaders betting the company on a new modality

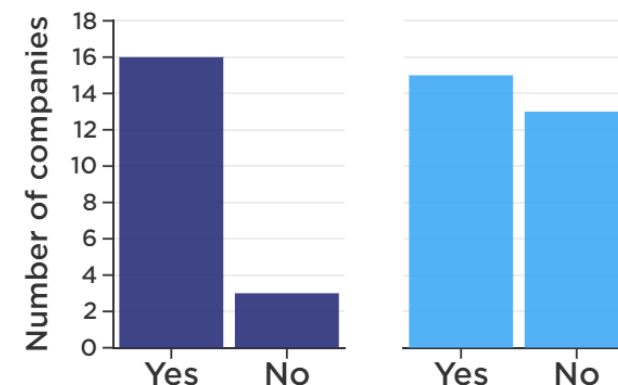
- ❑ 私营企业的**主导**项目里更有可能拥有全新用药模式，也更倾向于选择多样化的用药模式
- ❑ 4家上市公司拥有T细胞主导项目；在T细胞、mRNA、干细胞和双特异性药物方面，私营企业表现的很分散，其中双特异性药物是大部分企业的主导项目 (4)
- ❑ 上市公司可能并不依赖全新用药模式，但几乎所有 (84%) 企业都在打造全新用药模式项目，而私营企业在这方面的比例刚刚过半 (54%)

Private companies  
Public companies

### Lead program is new modality

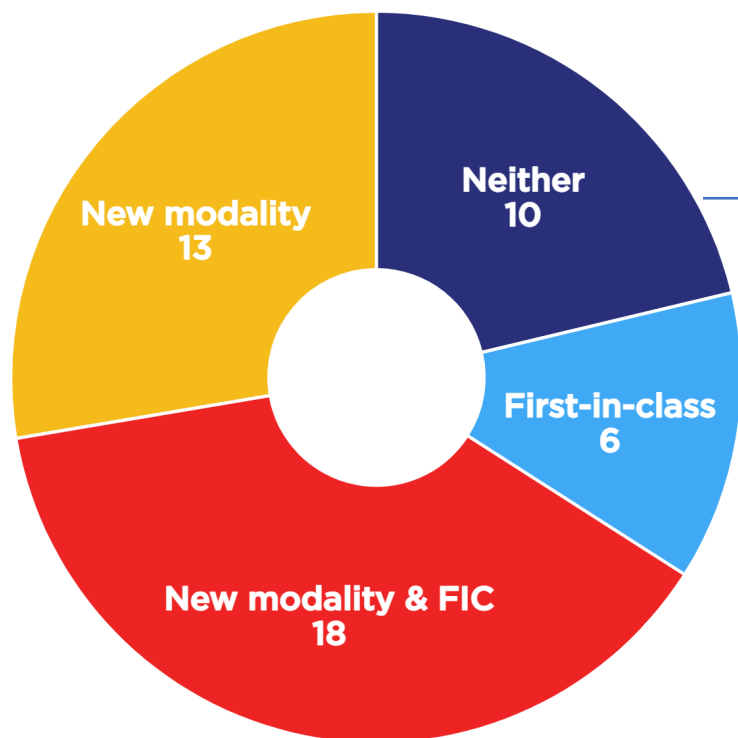


### New modality in pipeline



# Companies find alternative ways to shine

那些缺少 FIC 和全新用药模式的公司则通过其他价值实现的方式吸引融资

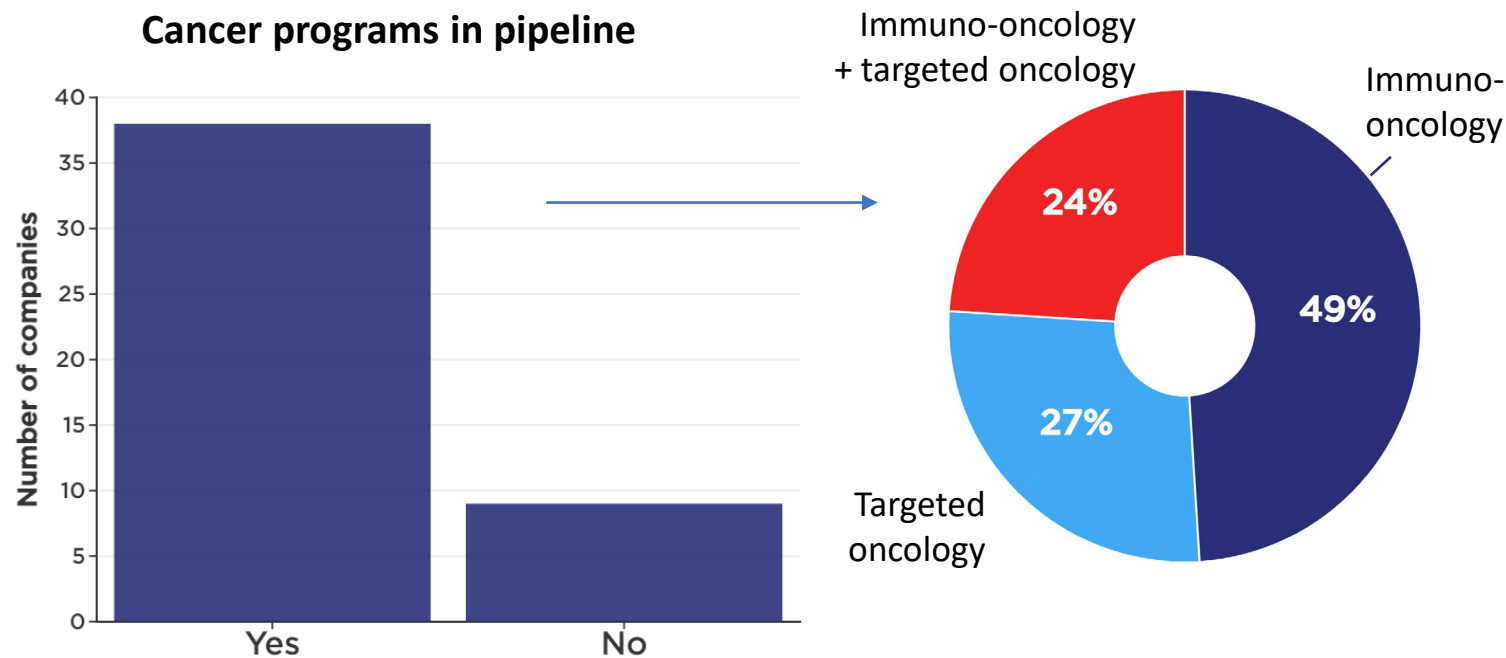


Strategies of companies without new modalities or FIC programs

Strategy	
Best-in-class	2
Fast follower	2
Innovative traditional modality platform	1
New preclinical targets	1
Delivery formulation	1
Undisclosed	3

# Is a presence in oncology still a must-have?

80% 的公司拥有至少一个癌症项目；其中 71% 属于肿瘤免疫学领域

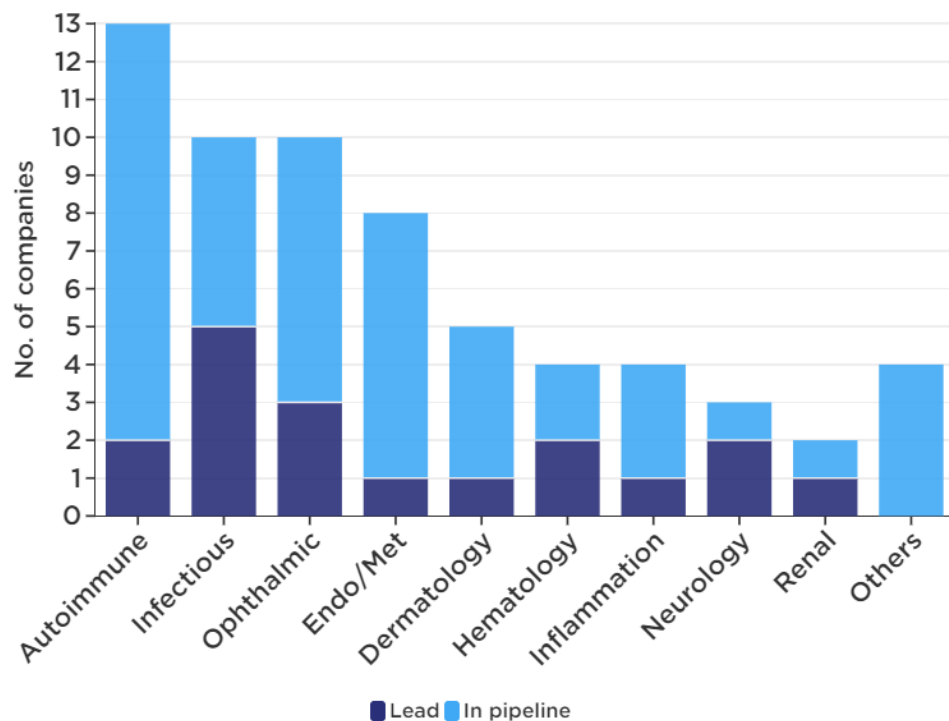


- ❑ 中国政府欢迎各方参与到癌症治疗领域，这样就可以在 NRDL 招标谈判中降低药品价格
- ❑ 投资者开始寻求差异化产品了吗？潜在领军企业中，有 20% 没有癌症项目

# China-prevalent diseases will dictate the agenda

随着研发治疗癌症药物公司的增多，更新型的生物技术公司细分到更多领域，以吸引投资

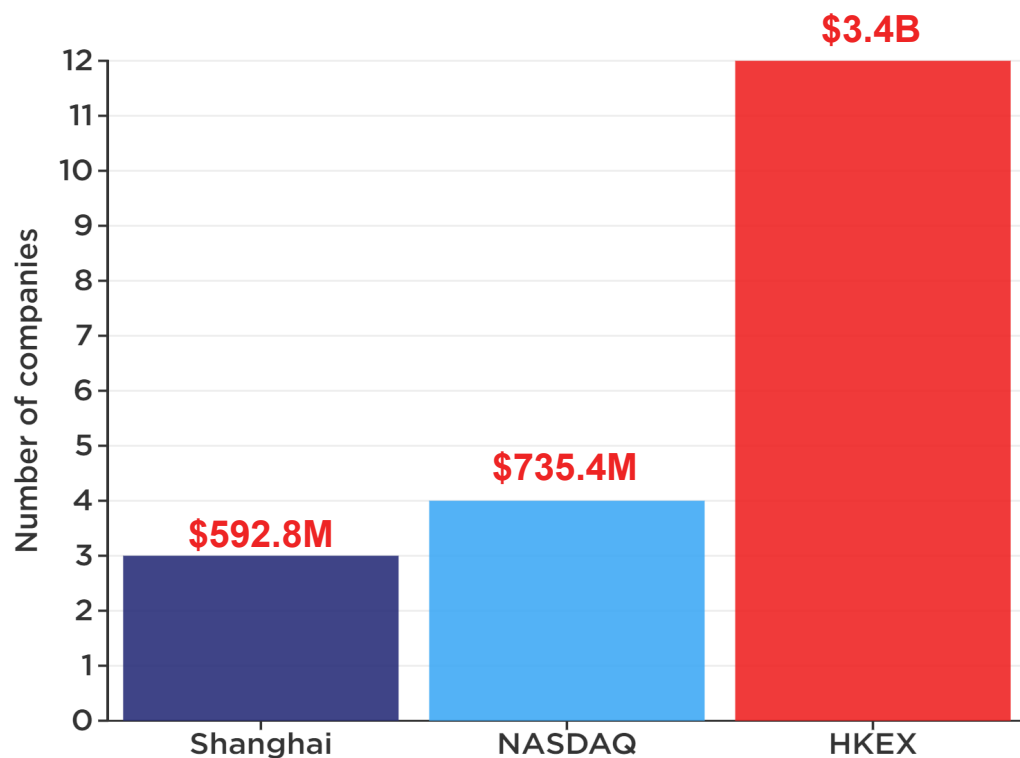
Non-cancer disease areas in company pipelines



- ❑ 中国的传染病防治成果远不止体现在新冠病毒方面
  - ❑ 10 家传染病防治公司中有 5 家公司专注于新冠病毒；这 5 家公司中有 4 家还有其他传染病项目
  - ❑ 主导项目还包括细菌性感染疾病、EB 病毒、流感、肺结核、艾滋病、狂犬病以及呼吸道合胞病毒
- ❑ 眼科疾病已跃居前沿，需要密切关注
- ❑ 中国对治疗自身免疫和糖尿病的需求可能会让内分泌/代谢公司与西方同样投资巨大的地区竞争
- ❑ 但是中国神经学疾病研究并未像美国一样再次出现热潮

## 未来的领军企业能在当地交易所找到全球投资者

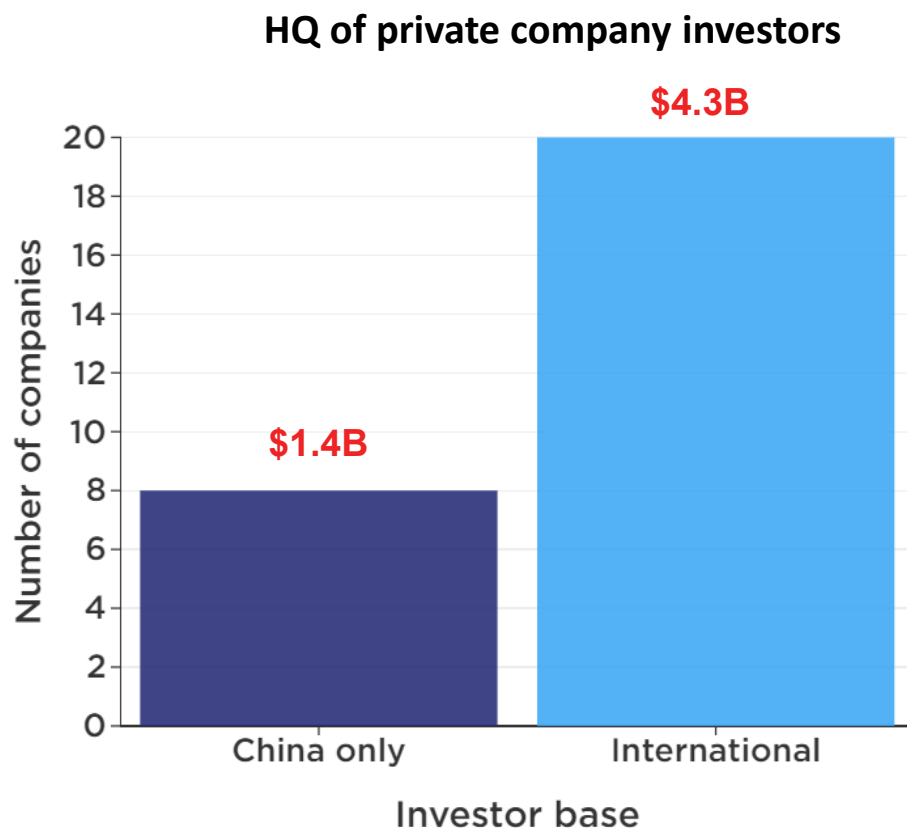
IPO exchanges for the public bellwether group



- 越来越多公司选择在香港上市这条被证明是好的路线
  - 未来领军企业在港交所的平均 IPO 是 2 亿 8340 万美元
  - 未来领军企业在纳斯达克的平均 IPO 是 1 亿 8390 万美元
- 越来越多的首批领军企业公司在两个交易所同时上市。新一代领军企业是否会寻求相同的优势还有待观察
  - 获得不同的投资者基础
  - 应对仅在纳斯达克上市的地缘政治挑战

# The broadening appeal of China's innovation

大部分私人领军企业候选者拥有国际投资人



- ❑ 71% 的未来领军企业背后有国际投资者支持
  - ❑ 不到四分之一的私营企业融资只来自中国财团
- ❑ 至少有 30 个不同的亚洲以外投资方正在资助中国新成立的公司
  - ❑ 3 家总部都位于新加坡
- ❑ 私营企业的投资者包括风投、对冲基金、主权财富基金、其他生物制药、私人股本和全球资产管理公司

## Thank You for Joining Us at The 8th BioCentury-BayHelix China Healthcare Summit!

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