

R&D Productivity – A Perspective for Chinese Biopharma Companies

A Value-Based View of R&D Productivity

R&D Productivity is an evergreen topic of senior executives in the biopharma industry, mostly in the context of what can be done to improve it. At Catenion we have almost twenty years of experience in helping companies from small biotechs to Big Pharma improve returns on R&D investments. Based on an old management saying – “you can’t manage what you can’t measure” it is important to create a definition that allows an objective tracking of productivity.

A lot of companies have no or very vague definitions of R&D productivity, mostly based on spending per new drug approval. Such a metric is typically a snapshot at a given point in time and does not reflect the five to ten years of R&D effort that go into novel drugs, and it also does not account for the actual value creation, as novel approvals differ widely in terms of commercial potential and net present value.

For those reasons, we have defined two R&D productivity metrics that reflect a more stable long-term perspective and a more snapshot like picture of current momentum. The metrics essentially capture the investment required to create the current pipeline and products launched in the last eight years. The two metrics are then weighted (long-term 3/4, momentum 1/4) and combined in an overall R&D productivity metric.

We also have a second set of metrics that looks at the commercial performance of companies, tracking growth rates of sales, EBITDA and market cap, both retrospectively and forecasted. This second metric is important as it shows how superior R&D performance ultimately translates into commercial success. The two metrics are then used to rank the largest 30 biopharma companies. Catenion has performed these rankings since 2014 on an annual basis, and in this year’s ranking we have included for the first time also smaller to mid-size companies (sales rank 30-50).

2021 Ranking – The Year of mRNA Vaccines

2021 has been a turbulent year for biopharma, with some very positive developments (eg. the success of mRNA vaccines for Covid19) and some problematic aspects (eg. the starting of the meltdown of US biotech valuations). For pharma the year has been good but not great, reflected in the comparably high number of approvals by the FDA (50 vs. 10 year average of 41) and stable share price performance.

Here is a summary of the 2021 ranking:

- mRNA vaccines top the ranking, both **BioNTech** and Moderna have been incredibly productive (spending vs. value created). Can Moderna and **BioNTech** “do it again” outside of infectious disease vaccines in the field of cancer or auto-immune disease & non-mRNA tech?
- China’s hidden champion **Jiangsu Hengrui** is in the top 5 the second year in a row. The key question is “can they move beyond best-in-class or me-too for China” strategy and become a real innovator? When will the post-Covid era start in China?
- **Vertex** lead drug Trikafta’s value keeps increasing, the question is can they move beyond their market dominating cystic fibrosis (CF) franchise? Long patent runway and good cash position give Vertex plenty of time to consider options to diversify.
- **Lilly** and **Novo** – GLP-1 agonists, the gifts that keep on giving. Especially Novo’s success and strategic fate, but also Lilly’s to some degree are linked to its GLP-1 franchises. The drug class started in T2DM, then came Obesity, and in the future possibly NASH.
- **Biogen** and **Eisai** – partners in Alzheimer’s disease, but under increasing pressure to make up for the Aduhelm flop.

- **Roche and Astra Zeneca** – Both traditional Big Pharma players with a strong Oncology dependence (>50% of portfolio value). AZ has started to diversify into rare diseases, also exemplified through the expensive Alexion acquisition, Roche has so far shied away from mega deals, in the past it could rely on a mixture of small to mid-size deals and its Genentech gRED R&D operation to fuel the pipeline.
- First ever ranking of mid-size companies (sales rank of 30-50) show some high-performers, with various degrees of strategic risk. Novavax (#1) will depend entirely on the fate of its Covid vaccine, whereas highly diversified companies such as BioMarin (#2) or Swedish Orphan Biovitrum (#4) combine a strong performance with a diversified rare disease portfolio.

Implications for Chinese Biopharma Companies

A Chinese company entered our ranking for the very first time in last year's survey as Jiangsu Hengrui made it straight to the top in its first showing as one of the largest 30 biopharma companies globally. In this year's ranking Hengrui made it to the #3 slot in R&D productivity and the #1 slot in company performance. So far, it is the only Chinese company in our top ranking because we look at the 50 largest companies by sales. However, we expect Beigene and perhaps a few others to enter the ranking in the future.

Chinese biopharma has gone through various phases, initially focusing exclusively on the Chinese market, often with drugs for highly precedent targets, this is now changing along two dimensions simultaneously – globalization and innovation. Jiangsu Hengrui is a good example of this, as the company's vision states that it wants to "Become a global biopharmaceutical group through innovation". Hengrui still has a way to go in the innovation area, as it is mostly focused on long-established targets, but overall China has established a strong position for example in the field of cell therapy, right now, there are more clinical studies for Car-Ts running in China compared to the US. While Chinese biopharma has traditionally mostly in-licensed assets for development in Europe or the US, there is now an increasing trend towards out-licensing assets as well. While this was historically mostly focused on Chinese rights, now Chinese are also taking on assets with global rights via overseas investment, merging or acquisition. One very recent case to notice is Sino Biopharmaceutical's acquisition of F-Star Therapeutics Inc. for its next generation bispecific discovery platform in June 2022. Grand Pharmaceutical Group is another good example, who successively acquired/invested Australia's Sirtex Medical Limited and ITM Isotopen Technologien München AG for their targeted radionuclide therapies.



研发生产力—中国生物制药公司的视角

基于价值的研发生产力观

“研发生产力”是生物制药行业高级管理人员的永恒话题，尤其是可以通过哪些措施来提升研发生产力。我们 **Catenion** 有近 20 年的助力从小型生物技术公司到大型制药公司提高研发投入回报的经验。基于一句古老的管理学理论——“你无法管理无法衡量的东西”，故，重要的是我们必须创建一个允许客观跟踪研发生产力的体系。

事实上，大多生物医药公司对“研发生产力”没有或者仅有模糊的概念，他们往往仅基于每个获批新药的研发支的制定评价标准。这样的指标通常是某给定时间点的一个快照，并无法反映新药研发 5 到 10 年的流程，也没有考虑新药实际创造的价值，因为获批的创新药物在潜在商业价值和净现值上存在很大差异。

出于这些原因，我们定义了两个评价研发生产力的客观指标，一组指标可反映稳定的长期视角，另一组指标更类似于基于某时间点的评价。这些指标基本上反映了当前研发管线和上市产品过去八年所需的投入。进一步我们对这两套指标进行加权（长期 $\frac{3}{4}$ ，当前 $\frac{1}{4}$ ），并将其组合成一个整体研发生产力指标体系。

此外，我们亦使用第二组指标，着眼于公司的商业业绩，跟踪销售额增长率、EBITDA 和市值，包含了回顾性和预测性数据。这一组指标很重要，因为它显示了卓越的研发绩效最终如何转化为商业成功。我们使用这些指标对全球最大的 30 家生物制药公司进行了排名。自 2014 年以来，**Catenion** 每年都会进行这些排名，发布于 *In Vivo Pharma Intelligence* 上。而在 2021 年的排名中，我们也首次将中小型公司也包括在内（销售额排名 30-50）。

2021 年排名—属于 RNA 疫苗的一年

2021 年对于生物制药行业来说是动荡的一年，这一年出现了一些非常积极的发展，例如针对 Covid19 的 mRNA 疫苗的研发成功；但这一年也出现了不少危机，例如美国生物技术估值开始崩盘。总体而言，对于制药行业来说，这一年综合表现不错，但不算优秀，这反映在 FDA 的批准数量相对较高（今年获批 50 项，而过往 10 年平均获批 41 项），同时股价表现也相对稳定。

以下是‘2021 年排名公布’的摘要：

- mRNA 疫苗位居榜首，**BioNTech**（拜恩泰科）和 **Moderna**（莫德纳）都展现了令人难以置信的生产力（支出之于创造的价值）。但是，这两间公司未来是否能在

非传染病领域，比如癌症或自身免疫疾病领域以及非 mRNA 技术领域中获得成功？

- 中国的隐形冠军**江苏恒瑞**连续第二年进入前五。其面临的关键问题是他们能否突破 best-in-class 或 me-too 战略，而成为真正的创新者？中国后疫情时代何时开始？
- **Vertex**（福泰制药）的主要药物 **Trikafta** 在创造不断增加的商业价值，它能否超越其主导的囊性纤维化特许经营市场？漫长的专利跑道和良好的现金状况使福泰有足够的时间考虑多元化的选择。
- **Lilly**（礼来）和 **Novo Nordisk**（诺和诺德）的 GLP-1 激动剂，可谓不断创造新价值的良作。尤其是主导了 Novo 的成功和战略命运；而对于礼来，在某种程度上其战略成功也与 GLP-1 特许经营权有关。这一类药物始于二型糖尿病领域，然后拓展到肥胖症，未来可能会进一步进入非酒精性脂肪性肝炎（NASH）。
- **Biogen**（渤健）和 **Eisai**（卫材）是阿尔茨海默病领域的长期合作伙伴，但目前两个巨头都在在弥补 **Aduhelm** 争议下的压力越来越大。
- **Roche**（罗氏）和 **Astra Zeneca**（阿斯利康）这两家传统的大型制药公司都对肿瘤治疗领域有很强的依赖性（> 50% 的肿瘤管线）。如今阿斯利康已开始向罕见病领域多元化发展，这也体现在昂贵的 **Alexion** 收购案中。罗氏迄今为止一直回避大型交易，它过往主要依靠中小型交易及其子公司 **Genentech**（基因泰克）的 gRED 研发业务为其扩充研发管线。
- 首次对中型公司的排名（销售排名 30-50 名）发掘一些高绩效企业，而他们也具有不同程度的战略风险。**Novavax**（#1）的成功与否将完全取决于其 COVID 疫苗的前景；而高度多元化的公司，如 **BioMarin**（#2）或瑞典的孤儿病公司 **Biovitrum**（#4）将高效的表现与多元化的罕见病产品组合相结合。

对中国生物制药公司的影响

一家中国公司在我们 2020 年的分析中首次入榜，这也是江苏恒瑞第一次成为全球最大的 30 家生物制药公司之一，且直接登上榜首。在 2021 年的排名中，恒瑞的研发生产力排名第三，公司绩效排名第一。到目前为止，恒瑞是我们排名靠前的唯一一家中国公司，因为我们基于销售额评价最大的 50 家制药公司。但是，我们预计百济神州以及其他一些中国公司不久的将来也会进入排名。

中国生物制药行业的发展经历了多个阶段，最初其专注于中国市场，并且仅仅针对已知靶点药物的开发。而目前看来，这两个维度同时在发生变化，中国生物制药企业在布局全球化并走入创新阶段。江苏恒瑞就是一个很好的例子，公司的愿景是“专注创新，打造跨国制药集团”。恒瑞在创新领域还有很长的路要走，因为它目前依然专注于长期确定的药物靶点。但宏观上，中国已经在制药业建立了强大的地位，例如在细胞治疗领域，与美国相比，中国正在开展着更多的临床研究。同时，商业拓展上虽然传统来看中国生物医

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药行业主要依靠从在欧洲或美国获得许可的资产进行开发(License-in)，但现在也有越来越多的向外许可资产(License-out)的趋势。除此之外，还有一个值得关注的趋势是，这些年，中国公司渐渐开始关注全球权益的资产，这体现在多个海外投资、收购和并购案例中，比如 2022 年 6 月发生的中国生物制药有限公司对致力于开发四价（2+2）双特异性抗体的 F-Star 公司的收购。另外一个例子是远大医药因布局靶向放射治疗技术先后对澳洲医疗公司 Sirtex 的收购和对德国 ITM 的投资。