CLUSTERS, MEGADEALS, "CELLICON VALLEY" AND THE "GOLDEN TRIANGLE"

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Whenever new technologies emerge, there are typically clusters of innovator companies, writes Dr David Seaward, 3P founder and Projects Director

Think about the first industrial revolution (1760–1830), which witnessed the exploitation of iron, coal and textiles in Britain. The world's first manufacturing town, owing its existence to that first paradigm shift in production, is Birmingham (now laying claim as the UK's second city). It's only 20 miles north of 3P's facility and, even now, some 200 years later, its industrial heritage lives on.

Similarly, California in the US-spawned Silicon Valley, where the silicon-based integrated circuit, the microprocessor and the microcomputer were all originally developed. The subsequently generated wealth has meant that Silicon Valley remains home to many of the world's largest high-tech corporations and thousands of start-ups.

So, where are the ATMP clusters? Currently, the two most dominant western countries in terms of ATMP development are the US and UK. Indeed, the area around Philadelphia, PA, is now known as "Cellicon Valley" ... an obvious nod to Silicon Valley. The term was first coined by Tmunity Therapeutics' co-founder in response to Philadelphia's gene and cell therapy development stronghold in the US.

In the UK, the area formed geographically by London, Oxford and Cambridge is known as the "Golden Triangle." Within it sits the GlaxoSmithKline site in Stevenage, part of which was redeveloped to be the UK government's Cell and Gene Therapy Catapult network. As intended, access to skilled pharmaceutical staff and lab space has acted as a catalyst to approximately £1.6 billion of ATMP investment within this zone.

Furthermore, it has recently been announced that the UK government will further fund the Cell and Gene Therapy Catapult's training centre and the UK's Precision Health Technologies Accelerator, both of which will be based in Birmingham to capitalise on the expertise at Birmingham University. The location, availability of world-class scientists and lab capacity will naturally accelerate the involvement of the West Midlands within the ATMP sector, which is already a leader in clinical trials work.

THE GOLDEN TRIANGLE

Rather than being just outside the Golden Triangle, 3P could soon find itself within the, ahem, "Golden Parallelogram," which, admittedly, is not such a catchy description!

Given the technological standing and population of the US, it's probably not surprising that America leads the world in terms of life science investment (and, by inference, ATMP research). Given the comparatively small population of the UK, it possibly is surprising that the country actually ranks third behind China (Table I). This is predominantly because of UK government support for research in the field and the fact that politicians and policy makers recognised that the sector had — and has — great potential for high growth and value-added jobs in the future.

Table I: Ranking for life science investment (2020)

One: US ~$31.9 billion (x3 in 5 years)
Two: China ~$4.1 billion
Three: UK ~$3.8 billion (x9 in 5 years)

The UK has a network of so-called Catapults; these are government-funded R&D establishments that sit between academia and industry. Their raison d'être is to provide a world-class facility for innovators and industry to try out new ideas and concepts. These "sandboxes" aid various industry players to "catapult" the UK's high technology sectors further and faster.

The Golden Triangle of UK life sciences

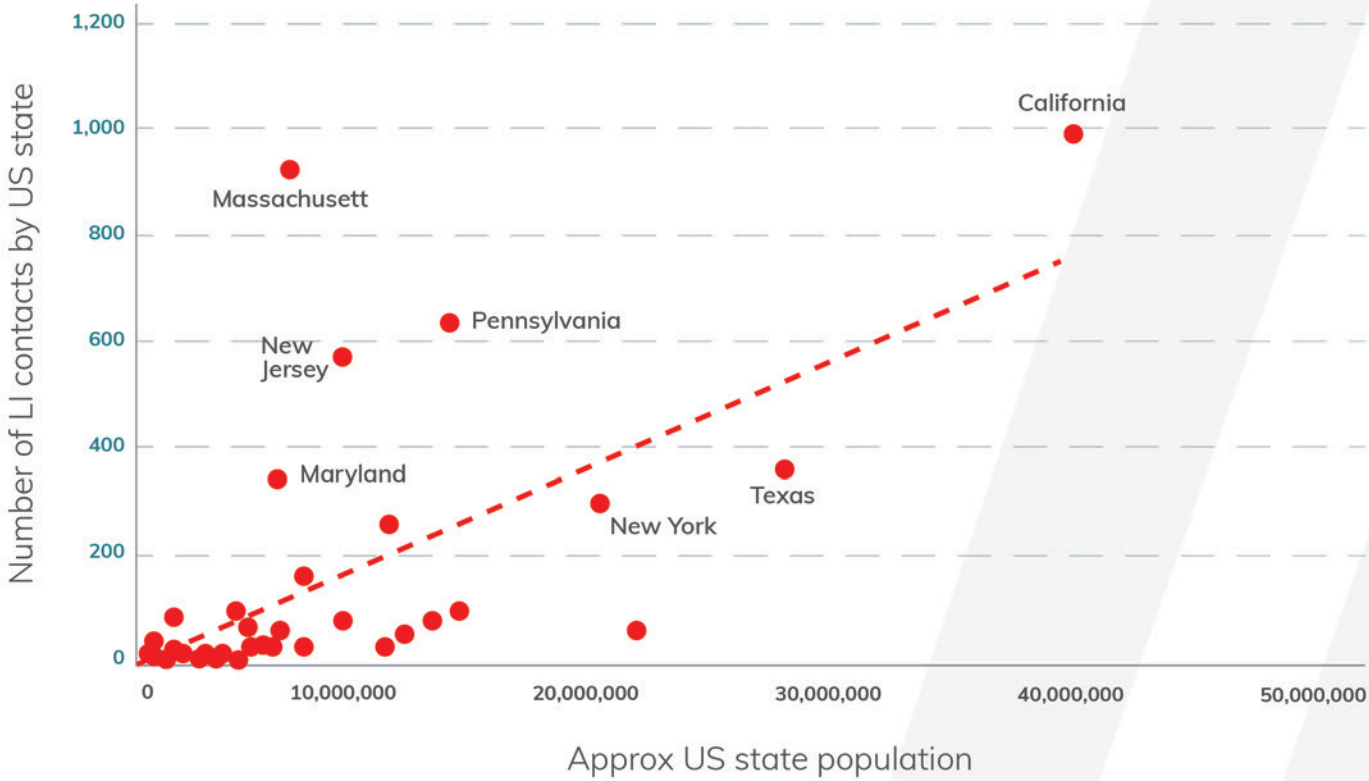
According to some LinkedIn-based research, using the authors profile as a basis, it's possible to dig a little deeper into the ATMP ecosystem and discover the locations of other global hotspots of activity. Given that LinkedIn claims to have around 800 million users and the author is a third-degree contact of nearly all of them, using either "cell and gene" or "ATMP" as a search filter, the top six most active countries are as follows:

- USA: 5200 contacts
- UK: 2000 contacts
- France: 1200 contacts
- Germany: 700 contacts
- Switzerland: 700 contacts
- Canada: 300 contacts

It's even possible to delve into a further level of regional detail. The following graph shows LinkedIn activity versus population for various US states.

Those above the dotted red line are "punching above their weight" in terms of their populations. Some are what the author intuitively understood from their activity but others were a surprise.

You can see that most activity is in California, Massachusetts, Pennsylvania and New Jersey.



MEGA DEALS

As an automation engineer, I've always subscribed to the mantra of "follow-the-money." The majority of the commercial equipment I've designed was for high value-added products within their respective sectors. 3P's engineers have played a significant role in the commercialisation of several blockbuster pharmaceuticals, which has subsequently led to us having a keen eye for large investment deals within the drug production sector. And, even by Big Pharma standards, the number and scale of ATMP-related is impressive!

As far back as the first modern biotech company, Genentech, records were being set. Genentech held its initial public offering in 1980, raising $35 million in the process. Share prices leapt from $35 each to a high of $88 within the hour: this was the largest stock runup ever seen in the US at the time. In 1990, Genentech merged with the "traditional" Swiss pharma giant, Roche, for $2.1 billion, with Roche acquiring 60% of Genentech's stock.

As such, Genentech had gone from start-up to the first "Big Biotech" in 14 years. Nearly a decade later, Roche bought the remaining stock and then reissued 19% (22 million Genentech shares). This was the largest healthcare public offering at the time. The stock moved from $97 to $127 a share within the first day of trading, valuing Genentech at $14.7 billion

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Roche had two more offerings in 1990, raising the share price to £163 and the value of Genentech to $18.9 billion. Bizarrely, Roche then made a hostile bid for the remaining Genentech shares in 2008 (valuing Genentech at $43.7 billion) but ultimately ended up paying $46.8 billion ... despite the market turmoil of the financial crash. Few biotech companies have had the success of Genentech. It is, however, a model that many biotech start-ups are following and is why investors flock to the sector.

The Alliance for Regenerative Medicine (www.alliancerm.org) produces reports on deals within the sector. By way of example, they collated the deals for the first half of 2021 (the last snapshot available, see Table II). This first-half reports totals investments of £14.1 billion (compared with full-year totals of £13.5 billion, $9.8 billion and $19.9 billion, respectively for 2018, 2019 and 2020).

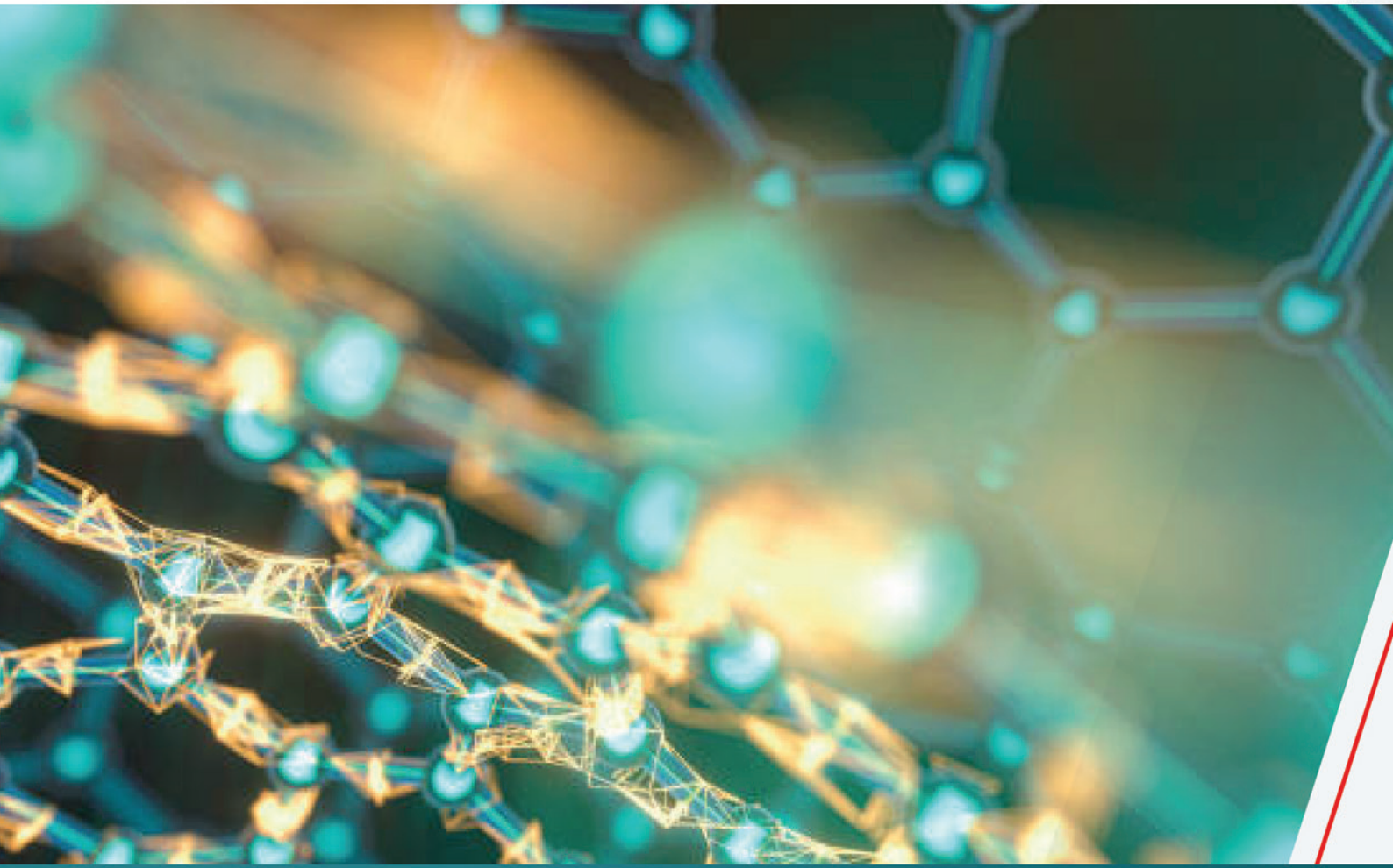

Table II:
>$100 million financing deals for the first half of 2021 (totals per section include all deals)

IPOS: £3.7 BILLION	FOLLOW-ONS: $2.5 BILLION	VENTURE CAPITAL: $5.4 BILLION	PRIVATE PLACEMENT: $1.0 BILLION	PARTNERSHIPS (UPFRONT DEALS): £1.5 BILLION
Sana Biotechnology: $675 million	Fate Tx: $432 million	Blackstone Life Sciences: $250 million	Beam Tx: $260 million	Vertex & CRISPR Tx: $900 million
Lyell Immunopharma: $425	Iovance: $350 million	Tessera Tx: $230 million	Orchard Tx: 150 million	Eli Lilly & Precision Bio: $135 million
CARsgen: $400 million	Editas: $231 million	Umoja Bio: $210 million	Mesoblast: $110 million	Ensoma & Takeda: $100 million
Instil Bio: $368 million	REGENXBIO: $230 million	Amplify Bio: $200 million		
Graphite Bio: $273 million	Generation Bio: $225 million	G2 Bio: $200 million		
Verve Tx: $267 million	Solid Bio: $144 million	Century Tx: $160 million		
Gracell Bio: $209 million	Adicet Bio: $137 million	Gyroscope Tx: $148 million		
Vor Bio: $203 million	Krystal Bio: $125 million	Jaguar Gene Tx: $139 million		
Achilles Tx: $175 million	Autolus: $100 million	eGenesis: $125 million		
Talaris Tx: $150 million		Artiva Bio: $120 million		
Decibel Tx: $138 million		Forge Bio: $120 million		
NexImmune: $126 million		Arcellx: $115 million		
		Caribou Bio: $115 million		
		Affinia: $110 million		
		Tenaya Tx: $106 million		
		Senti Bio: $105 million		
		Dyno Tx: $100 million		
		Scribe Tx: $100 million		
		TScan Tx: $100 million		

The investments can be stratified by type of therapy:

- Cell based immuno-oncology (such as CAR-T): $6.6 billion
- Gene therapy: $6.4 billion
- Cell therapy: $1.1 billion

According to the Alliance, there are 1195 companies currently developing ATMPs. In line with my LinkedIn analysis, 594 of these are in North America, 361 are in the Asia-Pacific region (dominated by China) and 209 are in Europe (dominated by the UK).

The size of the deals in this sector is large by any industry standard. The price of these treatments is also significant and could disrupt western healthcare systems. Much of the price is derived from the perceived value and associated with improved outcomes. There is also a cost of goods drag, which is driven by the complex and overly manual processes used in their manufacture. To paraphrase one ATMP senior executive, speaking to the author in 2021: "I know we charge £250,000 per therapy, as that's what we think the market will bear; but, at the moment, we're really struggling to make it for that! We desperately need more automation." Clearly, that's music to this MedTech engineer's ears.

THERAPY NAME	MANUFACTURER	INITIAL PRICE (US$)
Zolgensma™	Novartis	$2.1 million
Glybera™	UniQure	$1.2 million
Luxturna™	Spark Therapeutics	$860,000
Zolmoxis™	MolMed	$820,000
Kymriah™	Novartis	$480,000
Imylgic™	Amgen	$460,000
Yescarta ™	Gilead	$370,000
MACI™	Vericel	$40,000 (now withdrawn)

There are now conference papers available on the pricing strategies for these therapies. It's recognised that different and innovative reimbursement models will be required.

Plus, it's essential that patients receive the best care without being personally bankrupted or destroying their healthcare system, all while providing sufficient commercial incentive to continue with developing these amazing novel therapies.

This third blog has explained where much of the ATMP technology is being delivered, together with some insights as to why. Some historical context has been provided, as well as information on recent financing deals that help start-ups to fund their technical developments. The latest megadeals have been listed and stratified against therapy type and geography. Finally, some public domain pricing information has been provided.

Hopefully, the reader will understand why investors believe a significant return is to be made from these technologies. In the next (fourth) blog, the author sets the scene for automation with a reprint of a tweaked 2013 paper that discusses the costs and scale-up risks for medical devices.

Paper after paper, lists one of the primary constraints of the technology as the cost-of-goods, which is driven by complex manual processes. It is recognised that there is a real and present need for automation. Fortunately, some ATMP companies are taking the enlightened view that they need to develop the equipment and automation in parallel with the ATMP therapy itself.

To reuse the quote from a 3P client from the first blog in this series: "When you're trying to disrupt a $93 billion sector, it helps if you can actually manufacture your disruptive technology ... and this is where 3P come in!" The fifth describes how ATMPs are manufactured currently and what they future may hold for their automation.


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SELL
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