[TMO] Thermo Fisher

SCUTTLEBLURB
26 ABR 2023 · PAID

10

Share

Most of the time the subjects of my writing are more similar than they appear. They rhyme with or operate in the same ecosystem as something I've looked at in the past, so I can leverage prior knowledge to understand them. But every so often, as in the case of Dow DuPont or Nvidia, I cast a fresh line into unchartered ocean. You know how acquisitive companies will sometimes make a huge "platform" acquisition and then absorb lots of smaller companies into it? Likewise, I will sometimes publish a big post in a new domain and incrementally layer knowledge around that investment. Siddhartha Mukherjee's *The Gene* sparked my interest in genetics and cell biology when I encountered it some years ago and since then I've read just enough to place me firmly in the Dunning Kruger phase of the knowledge acquisition journey, where what I think I know vastly exceeds what I actually know. We're about to find what happens when a generalist dummy meets a dynamic industry saturated with product names he can barely pronounce in a domain he only superficially understands.

Then why do this at all? Because I think even industries that appear inscrutable to outsiders often contain a few pockets of activity that are amenable to analysis by a committed generalist. A company can be inside one's circle of competence even if it operates within an industry that largely falls outside it. In semiconductors I shouldn't be analyzing companies whose investment case is predicated on a technology bet or a turn in the inventory cycle. I'm not going to be the guy who calls the bottom in memory, I get that. But that doesn't foreclose Texas Instruments, whose hundreds of thousands of SKUs are designed into place for decades across a wide range of industries and where a 5+ year investment thesis doesn't require vigilant comparisons of feeds and speeds. Likewise, biotech and pharma companies are mostly outside my circle. I don't have the skillset to evaluate the progression of drug pipelines or assess the merits of new therapies. But the less sexy business of providing the instruments, ingredients, and

services that pharmas and biotechs use to develop and manufacture those drugs? That could work.

(This is the first part of a two-parter, with a short part 2 touching on Danaher, which has a very similar product mix, and maybe one or two others. Most of the substantive points are going to be here in Part 1).

Thermo Fisher reports in four segments.

Life Sciences

($ mn)	2014	2015	2016	2017	2018	2019	2020	2021	2022
Revenue	4,196	4,439	5,317	5,728	6,269	6,856	12,168	15,631	13,532
organic growth ex. Fx	*4%*	*5%*	*7%*	*6%*	*8%*	*10%*	*77%*	*23%*	*-12%*
EBITA	1,215	1,337	1,598	1,894	2,158	2,446	6,109	7,817	5,582
% margin	*29.0%*	*30.1%*	*30.1%*	*33.1%*	*34.4%*	*35.7%*	*50.2%*	*50.0%*	*41.3%*
Assets	19,257	17,884	19,065	19,063	18,774	18,306	20,209	22,751	21,848
EBITA / avg. assets		*7.2%*	*8.6%*	*9.9%*	*11.4%*	*13.2%*	*31.7%*	*36.4%*	*25.0%*
Capex	104	85	122	118	107	151	392	810	490

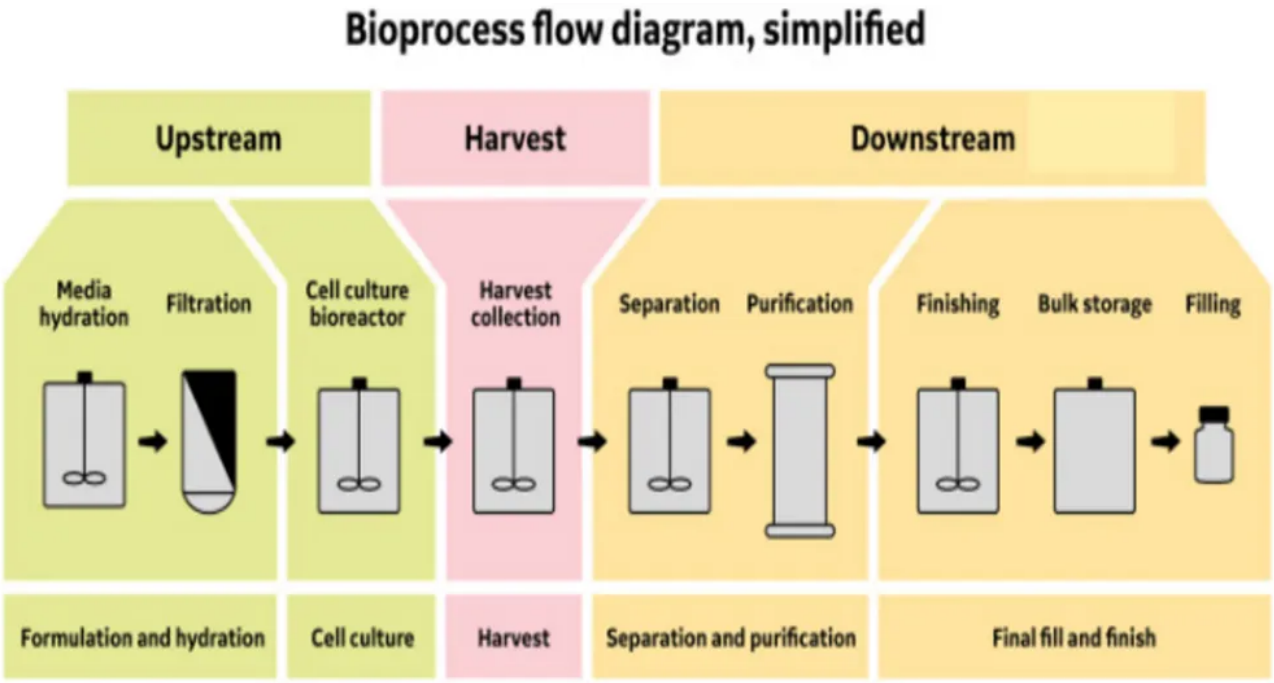
The Life Sciences segment was established in 2014 with Thermo's gigantic $15bn acquisition of Life Technologies, itself the product of the $7bn merger between Invitrogen and Applied Biosystems in 2008. Through this business, Thermo manufactures and sells instruments and consumables that researchers at universities, hospitals, and pharma/biotech companies use to discover, develop, and manufacture drug therapies.

You may recall the central dogma of molecular biology: information encoded in genes [1] is transferred to messenger RNA (mRNA), then translated into amino acid sequences that build up to proteins. Another way to say this is that genes *express* themselves in mRNA molecules and proteins. Those expressions change when a cell interacts with certain drugs. Those interactions can be monitored by PCR technology, which tracks changes in the concentrations of targeted mRNA pieces [2]. Thermo sells more than 2mn pre-designed gene expression assays, with primers that bind to specific nucleic sequences, as well as the reagents, wash buffers, and centrifuges needed to isolate RNA from cells and remove contaminants before the PCR process can even begin.

Beside PCR instruments and consumables, Thermo also sells flow cytometers that can be used to infer the size and shape of a cell based on how the laser light interacting with it scatters, as well as differentiate cells based on the colors emitted by the fluorescently labeled proteins on the surface of a cell as it passes through the laser. These instruments are also accompanied by a host of consumables, including filters that clear out cell debris; tubes that hold a variety of suspended cells; reagents and antibody kits to label the different protein permutations so they can be detected by the lasers; fluids that transports each individual cell through the flow cytometer at a constant rate; and tubes that collect the sorted cells after they pass through the laser.

Also included Life Sciences is a next generation sequencing machine (Ion Torrent), carried over from Invitrogen/Applied Biosystems, that can be used identify genetic mutations associated with diseases or link genes to the creation of certain proteins. The viral RNA sequence of SARS-CoV-2, for instance, was famously used to identify the gene that expresses the spike protein that binds to host cells, enabling the creation of mRNA vaccines [3].

Besides the instruments and consumables used to develop new drugs, Thermo sells the ingredients that pharmaceutical customers use to manufacture them. The bioproduction (or "bioprocessing") [4] work flow that converts living cells and their components into drug therapies is illustrated below:



Source: ScienceDirect

In a process called transfection, foreign DNA or RNA is introduced into cells to produce a certain enzyme, antibody, or other protein product that can be used to treat diseases. The goal of bioproduction is to collect those products, which can be excreted by cells or contained inside the cell itself. In other words, bioprocessing manufactures the cells that in turn manufacture the molecules we want.

But first you need…cells. Lots and lots of cells. In the Upstream phase, cell populations are fed carbohydrates, minerals, and dozens of other nutrients (cell culture media) until they grow large enough to be transferred to a bioreactor, a big steel drum in which the cells are fed more nutrients and continue to divide under a tightly controlled environment with exacting temperature, pressure, and pH levels. Increasingly, those bioreactors are of the "single-use" variety, where cells are nurtured inside a flexible plastic container within the steel drum. This does away with energy intensive sterilization routines, reduces turnaround times, and minimizes cross-contamination risk, as the plastic containers and related products are discarded after every batch. Danaher claims that single use technology cuts cost of goods by up to 30% and that the smaller manufacturing plants it enables results in a 40% lower upfront investment costs compared to traditional stainless steel setups.

After being nurtured inside the bioreactor, the cells are then separated from the pool of media and waste byproducts in the fermented broth. This gets us to the Downstream phase, where the molecules (proteins) are extracted from the cells themselves. The way this happens is the recovered cells are suspended in a buffered solution and pumped at very higher pressure through a tiny hole, causing them to rupture. The cell innards are then mixed with another solution and spun around in a centrifuge, which clears out cell debris and leaves behind the molecules of interest (lysate), which are then pumped through a filter to remove any remaining extraneous cell material.

But even after centrifugation and filtration, the lysate still contains various unwanted chemicals and proteins. To distill the solution further still, in the purification step the target protein is isolated using liquid chromatography, which can tell molecules apart based on differences in size (size exclusion chromatography), electric charge (ion-exchange chromatography), or attraction to water or some other molecule (affinity

chromatography). And finally, with the concentrated and purified therapy in hand, we reach the fill and finish step where vials are filled and packaged for distribution (for more details on the bioproduction process, I highly recommend this 3 part video series from BioNetwork).

Thermo-Fisher supplies products across all phases of the bioproduction process, though they are stronger upstream than they are downstream, with leadership in cell culture media (the nutrients required to grow cell populations) and single-use technologies (the plastic bags, seals, and hoses that are discarded with each manufactured batch).

Lab Products and Biopharma Services

($ mn)	2014	2015	2016	2017	2018	2019	2020	2021	2022
Revenue	6,602	6,662	6,724	7,825	10,035	10,599	12,245	14,862	22,511
organic growth ex. Fx	*5%*	*7%*	*5%*	*5%*	*9%*	*6%*	*13%*	*15%*	*10%*
EBITA	983	999	974	1,004	1,258	1,324	1,271	1,844	2,872
% margin	*14.9%*	*15.0%*	*14.5%*	*12.8%*	*12.5%*	*12.5%*	*10.4%*	*12.4%*	*12.8%*
Assets	10,876	10,267	9,405	19,181	19,051	21,761	22,711	52,639	51,281
EBITA / avg. assets		*9.5%*	*9.9%*	*7.0%*	*6.6%*	*6.5%*	*5.7%*	*4.9%*	*5.5%*
Capex	102	98	111	178	374	554	772	1,327	1,403

A life sciences company can turn to Thermo Fisher for the cell cultures, reagents, and single-used technologies needed to make drugs. *Or* they can just have Thermo Fisher's Contract Development and Manufacturing Organization (CDMO) manufacture those drugs for them. Like a hyperscale cloud or a semiconductor foundry, a CDMO acts as a centralized third party that can scale production across a variety of customers. More than 3/4 of biotech drugs in active development are from small, capital constrained companies that don't have the resources to build a globally distributed manufacturing footprint of their own. And large pharmas increasingly find it more efficient to outsource manufacturing while they focus on discovery.

According to Catalent, in 2021 biopharmas spend $165bn on drug development and manufacturing, with 40% of that outsourced to CDMOs, who seem to be grabbing about 1-2 points of share per year. Thermo Fisher hitched itself to this trend through the 2017 acquisition of Patheon ($7.4bn), establishing a presence in biologics (using cells to make active drug ingredients), followed by tuck-ins of Brammer Bio ($1.7bn; 2019) and

Henogen SA ($830mn; 2021), which focus on cell & gene therapy (transplanting living cells into patients and modifying DNA, respectively).

But when it comes to outsourcing, why stop at manufacturing? Thermo Fisher has long provided the logistics, distribution, and packaging for clinical trials but was averse to running clinical trials themselves. In 2018, when asked whether they would consider becoming a Contract Research Organization (CRO – a third party that runs clinical trials on behalf of pharma), management declared that it had "never seen [CRO] as a particularly strong fit with the company" and reminded investors that it divested the small CRO it used to own. But then 4 years later, Thermo acquired PPD, the 4th largest CRO, for $21bn, in its largest acquisition to date. I suppose this was only a matter of time, as the logic motivating Thermo's CDMO acquisitions applies just as well to CROs. As I wrote in my IQVIA post:

Declining R&D productivity, greater trial complexity, greater bargaining power from increasingly consolidated payers, growing generic drug penetration, and heavier regulatory demands are leading pharmas to conclude that running clinical trials, which was never a core function anyways, should just be outsourced to experts who can manage the process at far lower cost. This is especially true for small pharmas, who account for over 60% of all new drug approvals and don't have the resources to run trials in-house…

Large pharma sponsors, who still account for most of the industry's revenue, are concentrating spend on CROs who can design trials across a wide range of therapies in different countries and possess the data, technology, and infrastructure to efficiently design trials. This reality has prompted significant M&A transactions…

market share has been shifting to the largest CROs with global footprints as sponsors consolidate their third party relationships to gain purchasing efficiencies and pursue new drug approvals in multiple markets simultaneously (rather than sequentially) to get more bang out of their R&D buck. There are hundreds of CROs worldwide, but revenue is concentrated among the largest players, with the top 3 commanding ~40% market share, the top 7 close to 70%…

(The CDMO industry is relatively more fragmented, with the largest player, Switzerland-based Lonza, capturing ~11% share and #2 Catalent claiming another ~8%. In 2017, the

top 10 players, including Thermo Fisher, accounted for just ~35% of the market. Given the scale economies and pace of consolidation up and down the life sciences value chain, it's probably fair to assume that CDMOs will further consolidate too. I would expect Thermo to do more bolt-on acquisitions here)

Thermo Fisher doesn't consistently break out revenue constituents within the "Lab Products and Biopharma Services" segment but I roughly estimate that CRO (PPD) and CDMO (Patheon + Brammer) contributed ~$7bn and ~$3bn-$3.5bn last year, respectively, leaving the other ~50% of segment revenue coming from lab equipment (ultralow-temp freezers, cryto-preservation storage tanks, centrifuges, hotplates, stirrers) and consumables (flasks, pipettes, vials, solvents, chemicals, reagents).

Specialty Diagnostics

($ mn)	2014	2015	2016	2017	2018	2019	2020	2021	2022
Revenue	3,344	3,244	3,339	3,486	3,724	3,718	5,343	5,659	4,763
organic growth ex. Fx	*5%*	*3%*	*4%*	*4%*	*5%*	*5%*	*48%*	*5%*	*-13%*
EBITA	916	873	910	927	952	930	1,368	1,280	1,024
% margin	*27.4%*	*26.9%*	*27.3%*	*26.6%*	*25.6%*	*25.0%*	*25.6%*	*22.6%*	*21.5%*
Assets	8,048	7,183	6,802	7,095	6,663	5,867	6,534	6,010	5,542
EBITA / avg. assets		*11.5%*	*13.0%*	*13.3%*	*13.8%*	*14.8%*	*22.1%*	*20.4%*	*17.7%*
Capex	85	76	72	87	103	83	175	167	112

Some of the instruments and consumables used to discover and develop drugs can also be used to diagnose diseases. Here, Thermo Fisher restricts itself to relatively niche areas with less competition, like autoimmune diseases (arthritis, lupus, celiac disease); allergies (their blood analysis tests result in faster and more accurate diagnoses than applying an allergen on the head of a needle, pricking skin, and waiting for a reaction, an outdated method used in ~80% of allergy tests); transplants (to test for organ compatibility between donor and recipient…through One Lambda, Thermo has majority share of this niche market); and viral infections like COVID. The largest players in diagnostics are Danaher (through Cepheid and Beckman Coulter), Abbott, Roche, and Siemens. Thermo Fisher sells directly to reference labs and large hospitals but they also private label the reagents baked into the diagnostics products sold by the big 4.

Diagnostics is classic razor-razorblade. The idea is to expand the test menu and pollinate an installed equipment base with as many high margin assays as possible. Just as Canon ink cartridges only fit inside Canon printers, so too are Cepheid GeneXpert cartridges only compatible with GeneXpert systems, which in theory creates a captive long-lived annuity once you win the equipment sale. But this also seems insanely competitive space, with the big 4 and a long tail of others copy catting test manus and hop scotching one another on testing modalities and instruments.

Analytical Instruments

($ mn)	2014	2015	2016	2017	2018	2019	2020	2021	2022
Revenue	3,252	3,208	3,668	4,821	5,469	5,522	5,124	6,069	6,624
organic growth ex. Fx	*4%*	*4%*	*3%*	*9%*	*12%*	*3%*	*-8%*	*17%*	*14%*
EBITA	581	613	749	1,027	1,247	1,273	808	1,197	1,507
% margin	*17.9%*	*19.1%*	*20.4%*	*21.3%*	*22.8%*	*23.1%*	*15.8%*	*19.7%*	*22.8%*
Assets	4,133	4,763	9,520	9,960	9,907	9,896	9,773	9,692	10,019
EBITA / avg. assets		*13.8%*	*10.5%*	*10.5%*	*12.6%*	*12.9%*	*8.2%*	*12.3%*	*15.3%*
Capex	38	60	34	56	85	75	74	79	140

This is the most instrument-heavy/consumables-light segment of Thermo Fisher [5]. It is made up of 3 product lines: chromatography and mass spectrometry (~50%+ of 2019 segment revenue) [6], chemical analysis (10%), and electron microscopy (40%). Chromatography and mass spec have been around for a *long* time (the latter was developed nearly a century ago and was used to measure elemental atomic weights). Growth mostly comes from replacement demand, though there are ongoing efforts to expand the mass spec TAM beyond research labs by making them easier for non-specialists to operate in clinics and hospitals.

Liquid chromatography (LC) is a technology that separates molecules based on their size, electric charge, or affinity to a particular ion or molecule (ligands). Using the purification step of bioproduction discussed earlier as an example, the way this works is over *here* we have the lysate containing the target protein we want along with other kinds of proteins and molecules we don't want (mobile phase), and over *there* we have a steel column filled with glass or resin beads that are engineered to bind with molecules that carry certain physical attributes (stationary phase).

When the mobile phase is poured into the stationary phase, the target molecule is separated based on its size (small molecules will be trapped by small crevices in the beads while everything else will flow around the beads and leave the column first), electric charge (negatively charged molecules will bind to the positively charged beads), or attraction to receptors (the unique shape of the target protein locks to ligands on the beads). Gas chromatography (GC) is used for volatile molecules that more readily vaporize. Compounds are separated based on differences in boiling points rather than electric charge or ligand affinity. I'll spare you the details.

So, chromatography is good for separating molecules with different physical properties and the corresponding chromatogram will display the relative abundance of those molecules. But this doesn't actually tell you about the molecules themselves. That's where mass spectrometry comes in. Basically the way a mass spectrometer works is it shoots an electron beam at particles, dislodging electrons and creating ions. Those positively charged particles are accelerated through a magnet, causing them to travel along a path whose curvature is determined by the particles' mass/charge ratio. Plotting the mass/charge of ions against their relative abundance provides clues about the structure of different molecules. This technology is useful in drug development. In the early stages, it can identify proteins associated with certain diseases and track how the quantities of those proteins change in response to varying doses of drug therapies. During clinical trials, it can identify, track, and determine the structure of drug metabolites to guide dosing and predict efficacy. And during the manufacturing phase, it can detect impurities.

Earlier, I talked about how PCR could be used to amplify snippets of DNA/RNA associated with proteins. Siddhartha Mukherjee describes proteins as the "workhorses of the cell" in that they "form enzymes that control the chemical reactions of life. They create structural components of the cell. They are the receptors for signals from the outside. They form pores and channels across the (cell) membrane, and the regulators that switch genes on and off in response to stimuli" (from *The Song of the Cell*). Rather than infer the existence of certain proteins through DNA, which is complicated by the fact that a gene can express itself in various protein isoforms that have slightly different functions, researchers can use mass spectrometers to identity proteins directly. They do this by matching the mass spectrum of peptides (strings of amino acids that make up

proteins) against a database of candidate peptides to identify which proteins those peptides come from and are therefore which proteins are present in the sample. Proteomics is a relatively nascent but promising field that researchers seem very excited about, though there are still considerable technical challenges to analyzing proteins at high throughput. Some were saying "proteomics is the new genomics" 15 years ago too.

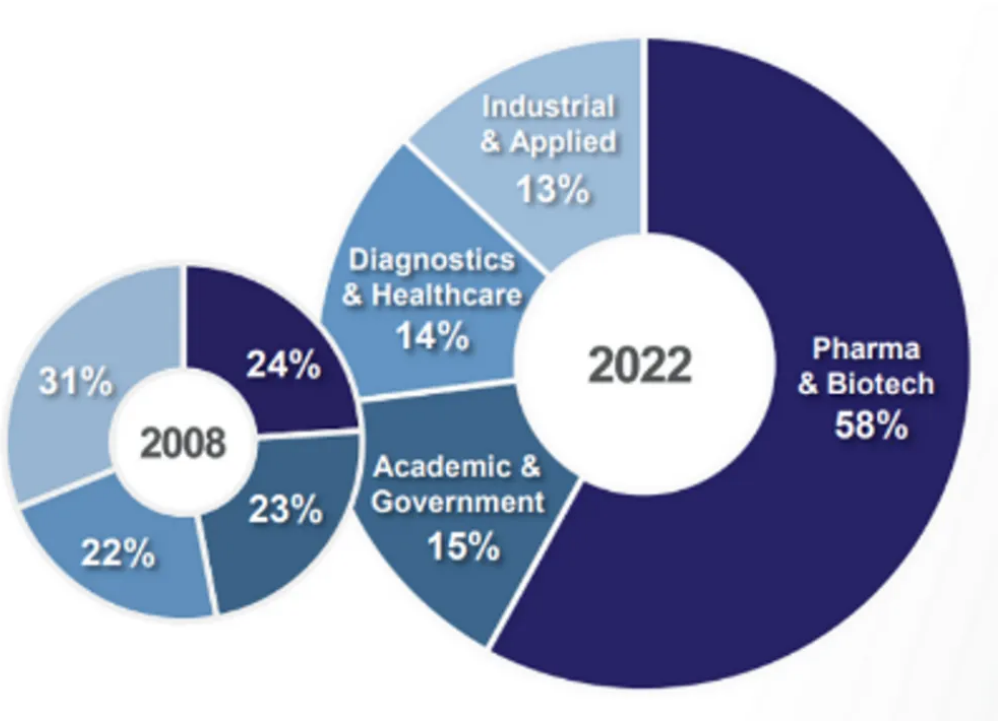
Anyway, with chromatography separating molecules and mass spec identifying them, the two technologies are complementary parts of the same workflow and often sold together as a single system (LC-MS or GC-MS). By most accounts, Thermo Fisher's Orbitrap mass spec is highly regarded and taking share from Waters, though Waters supposedly has the better high performance liquid chromatograph (HPLC). Competing systems are largely incompatible, which inhibits best-of-breed product selection.

Electron microscopes are the other big ticket capital equipment sold through this segment. Thermo Fisher established a major presence here through its $4.1bn acquisition of FEI in 2016 [7]. An electron microscope uses a beam of electrons to magnify objects, allowing them to resolve details at an atomic level (it was through the use of electron microscopes that researchers proved that the cell membrane was made up of two fat layers (a porous lipid bilayer) with proteins floating inside). They can be used to clarify the structure of proteins and viruses, as well as understand the impact of therapies on cells.

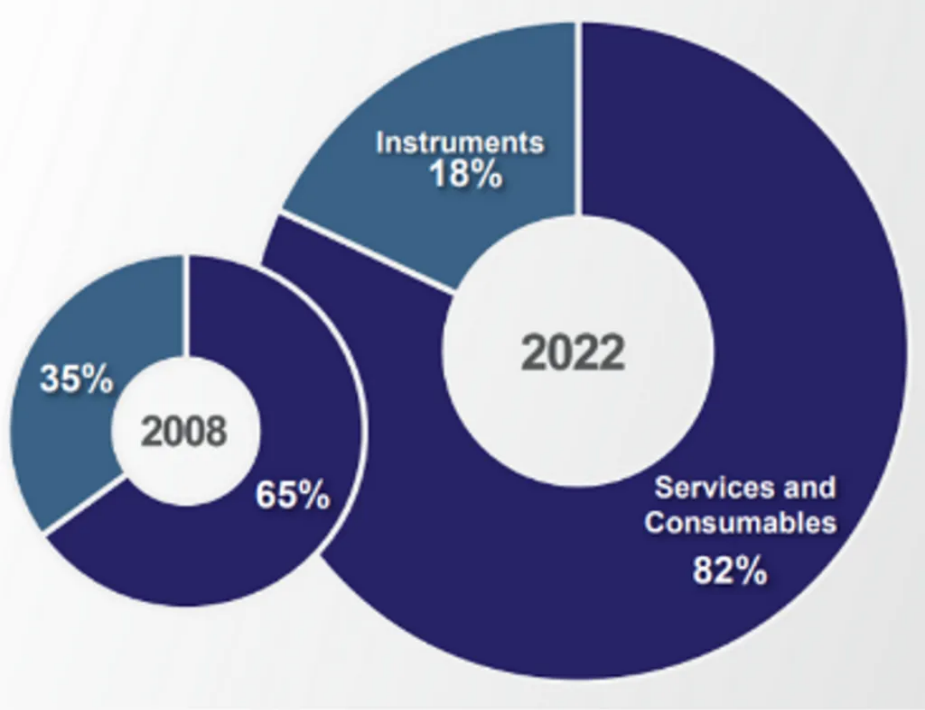
Finally, the Chemical Analysis subsegment is a grab bag of analyzers that use X-ray, infrared, and other radiation technologies to measure the thickness of steel and plastics, screen for lead in consumer products, identify explosive material, and measure air pollutants, among other industrial and environmental applications.

In a more general sense, many of the technologies discussed so far are designed to see tiny molecular objects and can be applied to a wide variety of markets outside life sciences. Electron microscopes are commonly used to identify defects in semiconductors and contaminants in soil and water. Chromatography and mass spectrometry are used by food producers to test for pathogens and by environmental agencies to detect harmful toxins in the air. PCR technology is used by police departments to amplify DNA found at crime scenes. But these are sideshows. The vast majority of Thermo's revenue comes from healthcare and life sciences. Pharma & Biotech – which had been growing

~9% organically in the decade leading up to COVID and mid-teens over the last 5 years – accounts for close to 60% of Thermo's revenue, with about half of that coming from production activities (bioproduction + pharma services), another half from pre-clinical research.



Close to half the company's revenue ($20bn) comes from recurring-ish consumables, ~70% of which are sold through fishersci.com [8] (the successor to the Fisher Scientific catalog that has been published for more than 100 years), an online store carrying 2.5mn+ products manufactured by both Thermo Fisher and 9k+ third parties. This business is often dubbed the "Amazon of scientific supplies" for its unparalleled breadth, though the stringent regulatory requirements and specialized cold chain logistics related to managing biological and hazardous materials offers protection from Amazon itself. Through United Lab Services, Thermo also services equipment and trains researchers on how to use it.



This smorgasbord of instruments and consumables is the byproduct of furious M&A activity that stretches back generations. But the foundational merger that set the foundation for all the others is the $11bn all-stock combination Thermo Electron and Fisher Scientific in 2006. Thermo Electron was a 50 year old vendor of scientific equipment and software headquartered in Waltham, MA. Fisher Scientific, 2x larger by revenue and 40% larger by market cap, was a 102 year old purveyor of reagents and consumables located 56 miles away, in Hampton, NH. That the two complementary entities would merge and provide a one-stop shop for customers through Fisher's distribution network made all the sense in the world.

Since then, Thermo Fisher has spent around $60bn on acquisitions (vs. a current enterprise value of $250bn). Here are the most notable ones (> $500mn):

Target	Date	Txn value ($bn)	Est. txn value / Rev	EBITDA	PF EBITDA*	Notes
Binding Site	1/3/23	2.7	10.8	NA	NA	Specialty Diag (multiple myeloma)
PeproTech	1/5/22	1.9	18.6	NA	NA	Reagents (recominant protein)
PPD	12/8/21	20.9	3.6	21.1	18.7	CRO
Henogen SA	1/15/21	0.8	8.7	NA	NA	CDMO (viral vector)
Brammer Bio	4/30/19	1.7	6.7	NA	NA	CDMO (viral vector)
Patheon	8/29/17	7.4	3.8	19.1	14.6	CDMO
FEI	9/19/16	4.1	4.2	18.3	13.5	Electron microscopy
Affymetrix	3/31/16	1.3	3.7	25.2	10.9	Gene analysis, flow cytometry
Life Technologies	2/3/14	15.3	4.0	12.8	10.4	Gene sequencing, cell culture, PCR
One Lambda	7/16/12	0.9	5.1	10.9	6.7	Transplant diagnostics
Phadia	8/23/11	3.5	6.7	20.4	17.0	Allergy diagnostics
Dionex	5/17/11	2.0	4.4	19.4	12.3	Liquid/ion chromatography

* includes synergies; txn value subtracts NPV of tax benefits

The one-stop shop logic motivating the foundational Thermo Electron-Fisher Scientific merger weaves through all these deals. It's a reach but maybe we can analogize Thermo Fisher to Microsoft? Microsoft supplies the infrastructure, code repositories, development environment, databases, monitoring tools, security…basically everything but the creative energy required for a developer to create software. They aren't necessarily the best in any single area…but what does being "the best" even mean? For the typical enterprise customer, the value of an integrated set of products that play well together is greater than the sum of their mediocre parts *and* greater than the sum of best-of-breed point solutions. This doesn't mean Microsoft can completely drop the ball on product and innovation, just that they have the leeway to be "good enough" in many areas because tight product integration does much of the heavy lifting. And with deeply entrenched relationships with just about every Fortune 1000 enterprise, they have a receptive audience for new products.

Likewise, Thermo Fisher can hardly claim superiority across the board. While they have the leading share in cell cultures, transplant and allergy diagnostics, and mass spec they lag behind in next-gen sequencing, liquid chromatography, and several other areas I'm sure. But researchers care about the overall efficiency of their workflow (preparing samples, analyzing samples, and interpreting the results) – which is tied to ease-of-use, field service, and product availability. Just as Microsoft products work best when coupled with other Microsoft products, so too are Thermo's reagents optimized for its own instruments, its mass specs optimally paired with its own liquid chromotographs [9]. And just as developers and engineers remain loyal to tools they were trained on, so too

do researchers habituate themselves to Thermo's instrument control and workflow software, like the Chromeleon Chromatography Data System (CDS).

Meanwhile the suits upstairs want the procurement ease that comes from consolidated relationships. Thermo Fisher, with its unrivaled product breadth and support infrastructure, can meet the joint needs of researchers and executives. They serve just about every biotech and pharma out there in some capacity and, when faced with a big enough product gap, can remedy the deficiency through acquisition, leveraging distribution and best practices to create immediate value. After $60bn of acquisitions and $11bn of R&D, Thermo has just about every conceivable product and service a customer might need, and can act as a reliable partner through every phase of the drug lifecycle. For instance, before it realized any product revenue, Moderna was sourcing consumables from Thermo to run experiments. Then they leaned on Thermo's CDMO services to manufacture mRNA COVID-19 vaccines.

One can take the one-stop shop slash end-to-end service thing too far. When Labcorp acquired Covance (a CRO) in 2014, they talked a big game about how real time diagnostic lab data could be used to improve trial design and speed patient enrollment. But after growing Covance by just low/mid-single digits over the next 7 years, Labcorp came under activist pressure and now finds itself in the process of spinning off this underperforming asset. At various points in Thermo's post-2006 history, investors puzzled over whether one acquisition or another made commercial sense. After PPD was announced, I found myself wondering whether a vendor that supplies consumables for clinical trials really had the right to run clinical trials themselves. Was this another Covance situation? Moreover, Thermo hasn't shied away from paying steep valuations to catapult to immediate scale in complementary domains – 19x fully synergized EBITDA for PPD, 15x for Patheon, 17x for Phadia. Binding Site and PeproTech were taken out at SaaS-like revenue multiples.

But they seem to make it work? Three years after being acquired, One Lambda saw "radically higher margins" and faster organic growth. The same goes for Life Technologies, FEI, and Patheon, whose low-single digit growth accelerated to high-singles, with synergies meeting or exceeding guidance. Phadia's operating margins were improved by 10 points, from 33% to 43%, over 6 years. At the time it was acquired, PPD was expected to grow high-single digits and accrete EPS by $1.40 in 2022. Instead, PPD

grew high-teens and contributed $2 of earnings per share, with management expecting "extremely substantial revenue synergies" in the "hundreds of millions of dollars" that will start bleeding into the P&L this year.

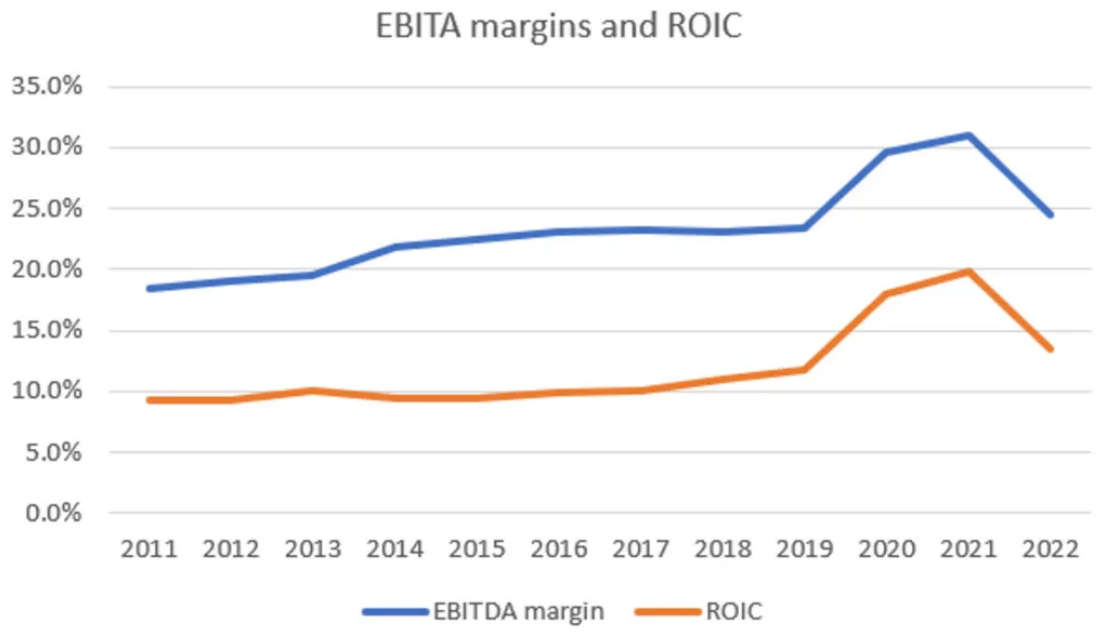
Besides the usual cost and revenue synergies – eliminating duplicative overhead, leveraging distribution and buying power, rationalizing manufacturing facilities, shifting production to low-cost regions – reflected in faster growth and higher operating margins, Thermo Fisher also takes advantage of its global footprint to extract tax savings on acquired profits, presumably through creative transfer pricing tactics. Reducing tax rates from 25% to 10%, as Thermo managed to do with Patheon, will result in serious earnings accretion, especially when paired with 1%-2% mid/long-term debt financing. Thermo wants acquisitions to exceed their WACC hurdle (8.5% in 2019) by year 4. They don't appear to have had much trouble consistently exceeding this goal.

Given the significant financial contribution of M&A, it should come as no surprise that improvements on one acquired asset after the next have translated into organic growth that has consistently surpassed internal expectations. From 2012 to 2014, Thermo guided to 2%-3% growth and produced 3%-4%. In 2015, they expected 4% "long-term" organic and surprised investors with 6% through 2019. On the back of those strong results, Thermo bumped the long-term growth target up to 5%-7%. Then COVID propelled them to ~low-teens over the next 3 years. Now they have ratcheted the long-term organic growth again, this time to 7%-9%.

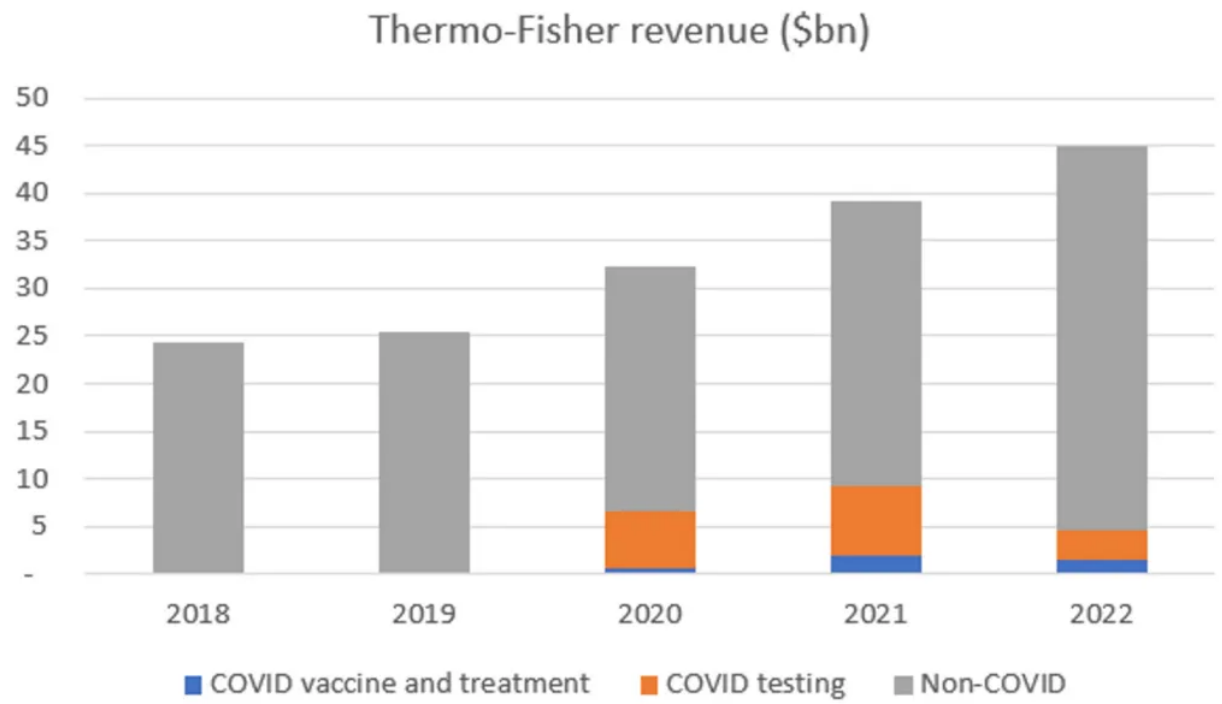
Management tells us that 7%-9% organic revenue growth should translate into ~40-50 bps of EBITA margin expansion going forward (in 2019, it took just 5%-7% growth to get the same 40-50 bps expansion. I'm assuming that lower incremental margins at PPD means more growth is required for the same margin expansion). Half that margin expansion (20-25 bps) comes from operating leverage and pricing. The other half from Thermo's Practical Process Improvement (PPI) business system, a *kaizen* practice of small ball problem solving and continuous improvement, initiated in 2002, that was clearly inspired by Danaher's celebrated Danaher Business System (DBS). In the case of FEI, PPI so profoundly reduced lead times at factories that revenue growth accelerated from 2%-3% to double-digits in just a year. The results of most PPI projects aren't nearly as dramatic of course but in an organization as large and sprawling as Thermo Fisher, the natural tendency is for bloat to insidiously infect the organization. You gotta have

something like PPI militantly enforced throughout. A corporate giant without rigorous calisthenic routines eventually buckles under its own weight.

So Thermo has long, credible history over surpassing expectation and in 2019, we might have expected ~50bps of margin expansion and ~100-120 bps of ROIC [10] accretion a year, absent M&A (pre-COVID, EBITA margins and ROIC were ~23% and ~12%, respectively). But then of course, COVID hit and profitability step-functioned higher:



In 2020 and 2021, around 22% of Thermo Fisher's revenue was related to COVID testing and treatment:



COVID-related revenue was halved in 2022. With instrument sales pulled forward and consumables inventory at customers being worked down, organic growth expectedly suffered:

Organic growth							
	2016	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**
Life sciences	7%	6%	8%	10%	77%	23%	-12%
Analytical instruments	3%	9%	12%	3%	-8%	17%	14%
Specialty diagnostics	4%	4%	5%	5%	48%	5%	-13%
Lab products and services	5%	5%	9%	6%	13%	15%	10%
Total	**4%**	**5%**	**8%**	**6%**	**25%**	**17%**	**0%**

Moreover, the tail end of the COVID hump also coincides with the withdrawal of easy money, leaving small biotechs with early-stage pipelines strapped for funding, with knock-on consequences for CROs, who in past years pointed to small biotech development as a growth driver. Finally, it is taking longer than expected for customers to destock excess bioprocessing inventory built up during the pandemic.

But these valid concerns are mitigated by several factors. First, during the pandemic established leaders like Cepheid (owned by Danaher) couldn't meet the influx of demand for respiratory PCR diagnostics, opening the door for Thermo Fisher, who was a bit player at the time. Thermo disseminated to clinics qPCR sample prep and

instruments that had up to then mostly been relegated to research labs, briskly capturing a "very large share" of worldwide qPCR testing. They also acquired PCR provider, Mesa Biotech, to expand their diagnostics presence at the point-of-care. Now, with COVID testing peeling off, this apparatus can be repurposed toward HIV, tuberculosis, and a growing number of other infectious diseases. The huge installed base seeded during the pandemic will pay a growing consumables annuity for years to come.

Second, the expanded bioproduction [11] and outsourced manufacturing capacity added over the last few years was not COVID-specific and will be absorbed by other therapies (though from what I understand the upstream products themselves, like cell cultures and single use technologies, tend to be drug-specific). This shouldn't take very long as even prior to COVID, revenue from bioproduction and outsourced services was growing 20% and "double-digits", respectively.

Third, biotechs with promising discoveries and precarious financials are prime acquisition targets for big pharma, who has long relied on early stage biotech to replenish their pipelines and may be especially inclined to do so now with target valuations re-setting lower. Even after experiencing explosive organic growth in the COVID years (+15% in 2020, +35% in 9m21), PPD, under Thermo's ownership, grew high-teens in 2022.

Fourth, Thermo Fisher has long promoted itself as a "trusted advisor", a claim that was tested and validated during COVID, as the company expanded capacity on short notice to accommodate testing and vaccine production amidst severe supply shortages. And unlike Catalent, their outsourced manufacturing operations weren't plagued by equipment malfunctions and deficiencies.

But above all, secular tailwinds are durable and intensifying. We appear to be on the cusp of a golden age in cell and gene therapy (CRT). Cell therapy introduces properly functioning cells into a patient while gene therapy modifies a patient's DNA. Whereas traditional small molecule drugs are synthesized from chemicals, and biologics, like monoclonal antibodies, are mass produced by and extracted from cultured cells, CGT modifies actual genes, which means it can effect permanent changes. So with CRTs, it is cells and viruses and gene-altering enzymes, rather than chemicals and purified proteins, that are injected into the patient. For instance, researchers at Verve Therapeutics use

lipid nanoparticles to deliver to liver cells gene-editing enzymes, enabling them to metabolize LDL cholesterol. This obviates LDL-cholesterol lowering drugs like Lipitor that need to be taken every day for the rest of a patient's life.

Sometimes, as in the case of bone marrow transplants to treat leukemia, donor cells are transfused without introducing or modifying genes. Other times, cell and gene therapy are part of the same overall process. In the case of 4-year old Ashanti DeSilva, who suffered from a rare mutation on a gene called ADA – which codes for an enzyme that converts adenosine, a naturally occurring chemical that produces toxic metabolites, into an innocuous product – a team of gene therapists at the National Institutes of Health introduced an ADA-carrying virus into T cells extracted from DeSilva's blood and re-introduced those infected cells back into her body. This was in 1990. The results were promising and sparked a frenzy of excitement about the possibility of using CRT to treat genetic diseases like Huntington's and cystic fibrosis.

Nine years later, a similar procedure was performed on Jesse Gelsinger, whose genetic mutation prevented the production of an enzyme involved in the breakdown of proteins, leading to a toxic build up of ammonia. Except this time, rather than modify cells outside the body (ex vivo [12]), viruses carrying the functional gene were introduced directly into Jesse's body (in vivo), where they infected the liver cells that normally synthesize the protein-dismantling enzyme. Jesse tragically experienced a severe immune response to the virus and died. Congress huffed, the FDA canceled nearly all outstanding trials, and the field of gene therapy stagnated for the next decade.

But researchers got a better handle of viral vector safety and other delivery mechanisms [13], and the deep freeze gradually thawed against the lambent glow cast by a series of successful gene therapy trials, culminating in the FDA approving the first US gene therapy, Novartis' Kymriah (reprogramming T cells to fight follicular lymphoma), in 2017, 5 years after the first gene therapy was approved in Europe.

Meanwhile gene-editing became more reliable and exacting. No method has garnered as much celebrity as CRISPR-Cas9, in which RNA guides the Cas9 protein to matching sequences of DNA, to which it can make precise insertions, edits, or deletions. From the incomparable Siddhartha Mukherjee:

"Imagine, for a moment, the entire human genome as a vast library. Its books are written in an alphabet containing just four letters: A, C, G, and T, the four building-block chemicals of DNA. The human genome has 3 billion such letters – 6 billion per cell if you count the genomes both parents. Reframed as a library of books, with about 250 words per page and 300 pages per book, we might think of ourselves – or rather the instructions to build, maintain, and repair ourselves – as written in about 80,000 books. Cas9, when combined with a piece of RNA to guide it, can be directed to make a deliberate change in the human genome. You can analogize it to finding and erasing one *word in* one *sentence on* one *page in* one *volume of that eight-thousand-book library…*

More recently, the system has been modified not only to erase words but also to implement a vast array of potential changes in a gene, such as adding new information or making more subtle alterations. Cas9 is a search-and-destroyer eraser. To continue the analogy, it can change "Verbal" to "Herbal" in the preface to volume one of Samuel Pepys' Diary in a college library containing eighty thousand books. Every other word, in every other sentence, in every other book in the library is, for the most part, left alone.

(excerpt from *Song of the Cell*)

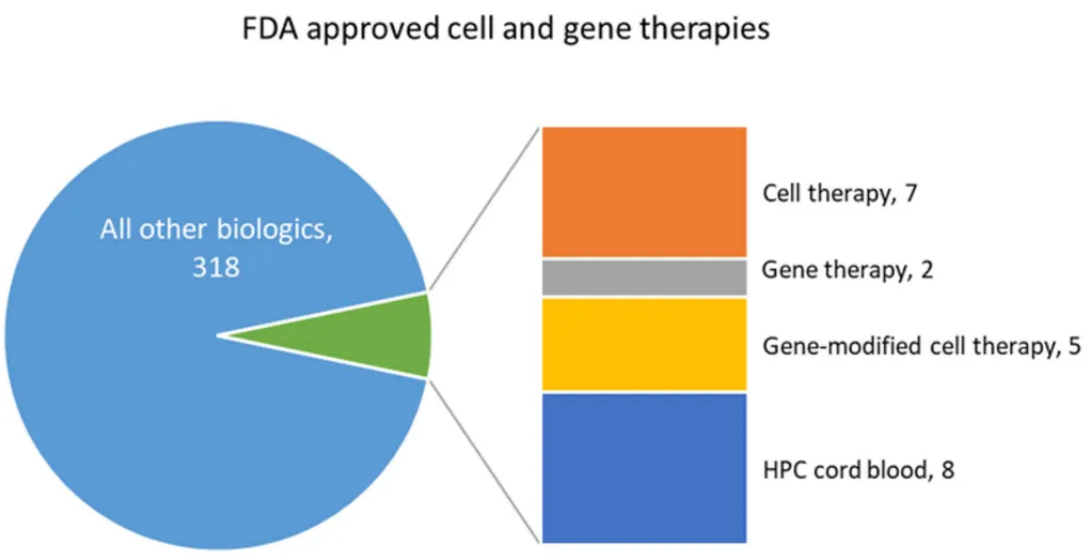
In 2019, stem cells were extracted from a 34-year old woman afflicted with sickle-cell disease and edited with CRISPR-Cas9 to produce normal-shaped red blood cells. Walter Isaacson describes the outcome in *The Code Breaker*:

In June 2020, [the patient] got some even more exciting news: the treatment seemed to be lasting. After nine months, she still had not suffered any sickle-cell pain attacks, nor did she need any further blood transfusions. Test showed that 81% of her bone marrow cells were producing the good fetal hemoglobin, meaning that the gene edits were sustained.

(for more on gene therapy, I also recommend *The Gene* by Siddhartha Mukherjee, a marvelously written book)

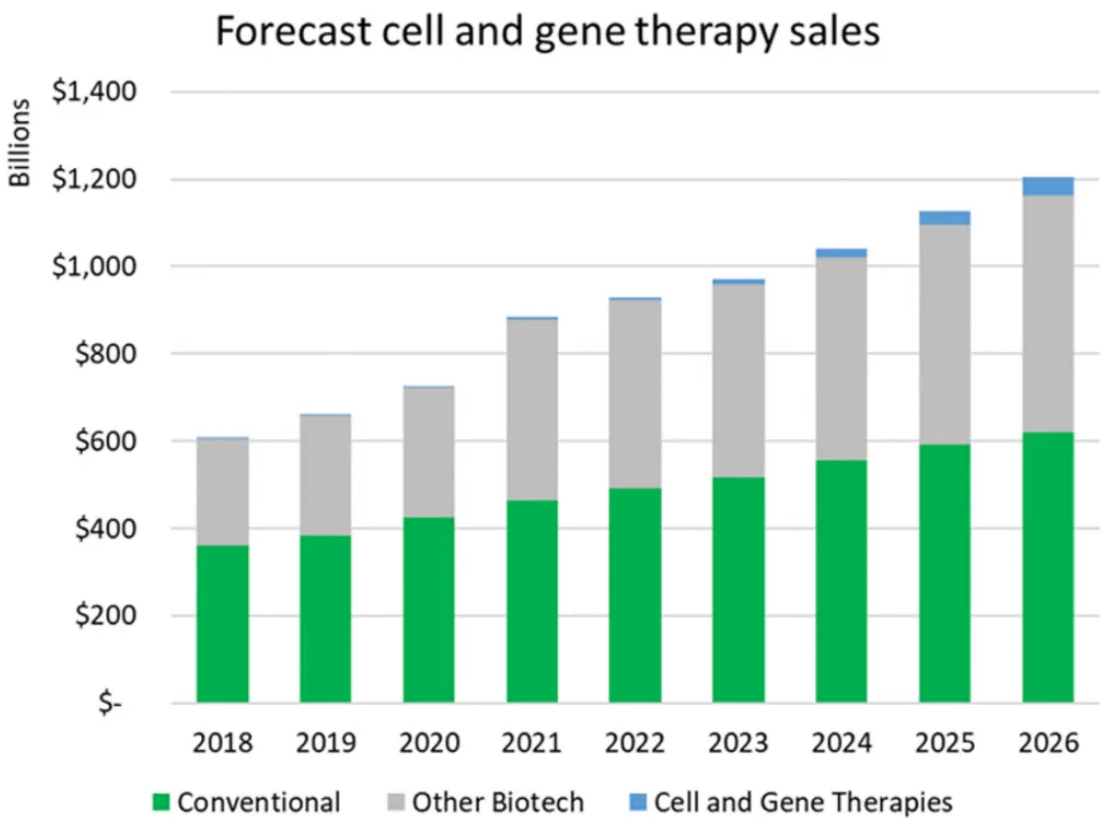
I'm astonished by this technology. How can you not be? And yet, for all the press CRT has gotten over the years, commercial progress has been slow.

FDA-approved cell and gene therapies are a small piece of the biologics pie….



Source: FDA and Evaluate Pharma

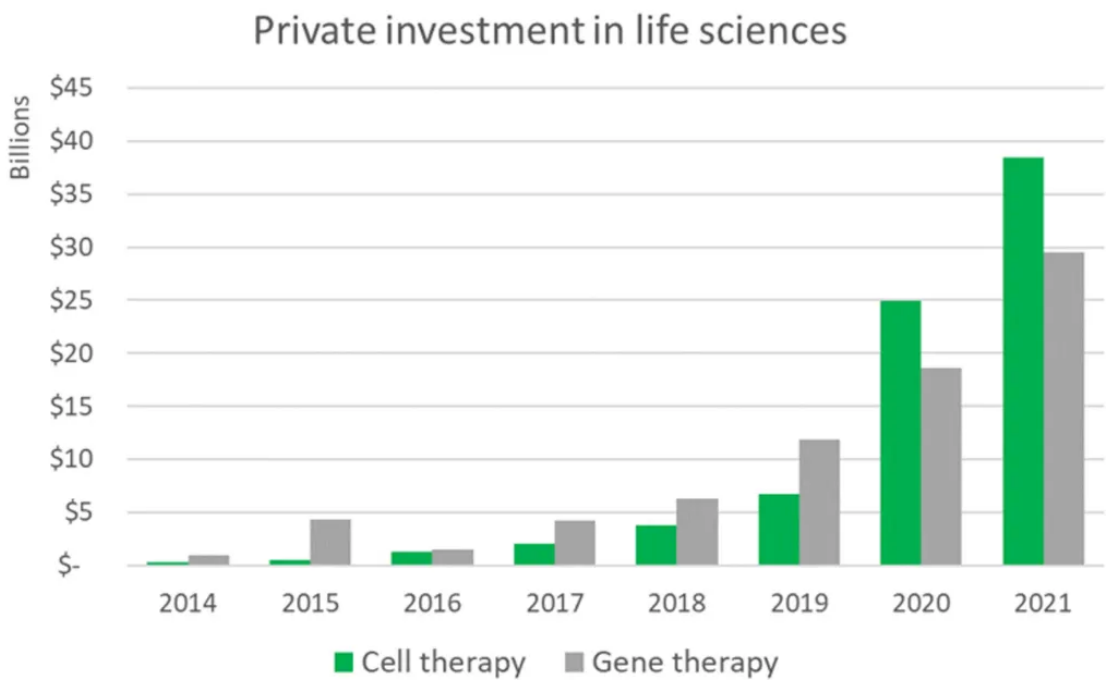
...and a negligible fraction of pharma sales:



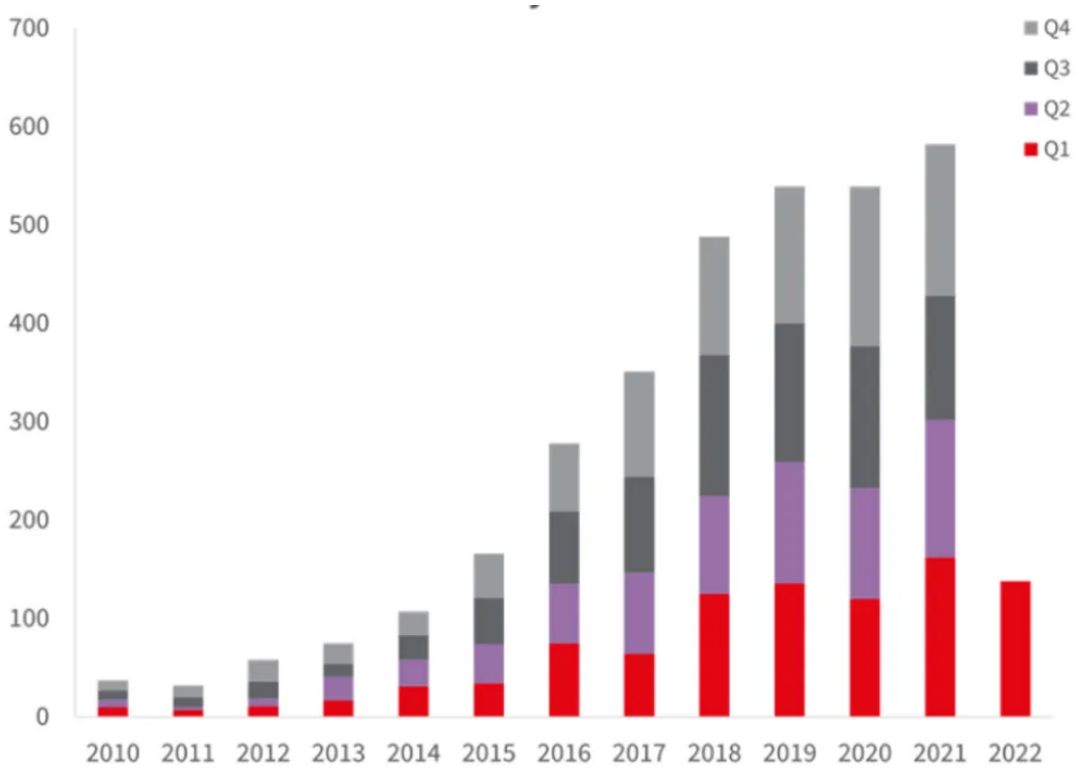
Source: Evaluate Pharma

CGTs are very complex, expensive, bespoke procedures [14] that are hard to scale and covered by unsettled reimbursement models. For now, gene therapy is mostly limited to

certain cancers and rare diseases [15]. Still, these novel therapies are compelling enough that, despite numerous challenges, they have attracted record sums of private investment:



The number of clinical trials for CGTs has exploded over the last decade:



Source: Global Data

Aided by enthusiastic support from its government, China has registered the third most clinical trials for gene therapy. Thermo's revenue from here has grown by mid-teens over the last decade. The US FDA had approved just 23 cell and gene therapies as of March 2022, but at the time there were close to 3,500 therapies in development. And while CRT is expected to be a small a fraction of overall pharma sales through 2026, according to Evaluate Pharma, its 62% 5-year CAGR far exceeds the single digit growth of conventional drugs and implies more than $45bn of annual sales. Thermo Fisher supplies the regents, gene editing tools, and outsourced services needed develop, test, and manufacture these high growth therapies.

Management expects long-term organic revenue growth of 7%-9% (50-100 bps from pricing). This is higher than any long-term guidance they've given since at least 2006 but given Thermo's long history of overshooting growth expectations, I'm inclined to give them the benefit of the doubt. Besides, 7%-9% doesn't requires heroic assumptions. Revenue from Industrial and applied applications grows at maybe 3%-5% but comprises just 13% of revenue. The traditional life sciences complex probably grows ~4%-5% over the next 5-10 years and CGT maybe contributes another point. Bake in some share gains and, voila! Another way to cut it is the 60% of Thermo that comes from Pharma and

Biotech should grow somewhere between, say, 9% (as it did pre-COVID) and 12% while the other 40% grows 4%-5%, which blends out to 7%-9%. Moreover, while exposed to idiosyncratic dynamics like COVID comps, excess inventory, etc., the life sciences complex is recession-resilient. Thermo saw its revenue contract by just 3% organically in 2009. Ex COVID, they might fare even better this time around, with just half as much exposure to instruments and industrial end markets today as they had in 2008.

One way to approach valuation is to forget about M&A and just assume 7% organic growth and 40 bps of annual margin expansion, which implies a ~high-teens ROIC by year 5. Including the cash build and slapping a 20x multiple on earnings gets you annualizing ~9% on the stock ($526) over the next 5 years. But this a somewhat misleading framework since in a space as dynamic as this some unknown portion of M&A will be required just to sustain organic growth. I touched on this in my Ansys writeup from 3 years ago:

No single simulation or CAD vendor will always have the entire toolkit to anticipate the ever-expanding needs of OEM clients, so acquisitions will always be part of the story for any company in this space. Sometimes these acquisitions turn into vital and strategic value drivers (PTC's acquisition of ThingWorx; Dassault's acquisition of Solidworks), but most of the time, as in the EDA space, we should think of acquisitions, especially the smallish tools-centric ones, as a recurring R&D expense, required to remain technically on par with acquisitive competitors.

If Thermo Fisher swore off acquisitions in 2016, what would their organic growth look like today? If they halted acquisitions today, what would organic growth look like in 5 years? I don't have a good way of parsing this out. But with big platform assets like Life Tech and Patheon rounded out with bolt-ons, it just seems that some of Thermo's acquisition spend should probably be considered maintenance R&D.

Key to the investment case for Thermo Fisher and Danaher is both companies are superior owners of life sciences assets. Like Danaher, Thermo accelerates profit growth at acquired companies through systematically executed kaizen. But Thermo Fisher's $44bn of revenue now supports $230bn of enterprise value. This is a huge company with enough share in certain pockets to warrant anti-trust scrutiny (Thermo will say they only have 20% share of a $200bn+ TAM, but the market is made up of lots of heterogenous

pieces in different states of consolidation). Also, assuming 35% of free cash flow is returned shareholders and a leverage ratio of 2.75x, Thermo will plow $50bn into acquisitions over the next 3 years. And if the last few years is any guide, they will do so at historically steep multiples. Now, they can justifiably outbid others because of their distribution might and disciplined execution. But this was just as true in 2014, when they paid just 10x synergized EBITDA for their $15bn acquisition of Life Technologies, as it is in recent years, where they find themselves paying 19x for the $21bn acquisition of PPD and double digit revenue multiples for PeproTech and Binding Site. As is always the case with acquisitive concepts, Thermo is as much a bet on disciplined capital allocation as it is on the attractive attributes of the underlying business.

Disclosure: At the time this report was posted, accounts managed by Compound Insight LLC owned shares of TXN and MSFT. This may have changed at any time since.

---

1 sections of DNA sitting inside the cell nucleus that code for certain proteins

2 technically, the mRNA pieces are reverse transcribed into more stable complementary DNA (cDNA) that are then read by the PCR machine

3 NGS a tiny percent of the company's revenue and their technology continues to significantly lag the market leader, Illumina

4 Bioproduction accounts for ~10% of Thermo's revenue

5 at the time it was acquired, electron microscope maker FEI got 70% of its revenue from equipment sales, with most of the remaining from services rather than consumables

6 in 2009 Life Technologies, which was acquired by Thermo Fisher in 2013, sold its mass spec business to Danaher for $450mn, citing the technology's minimal consumables trail

7 they had a definitive agreement to acquire Gatan, an electron microscope manufacturer, from Roper Technologies for $925mn but the deal was scuttled by anti-trust concerns. Gatan was later acquired by Ametek

8 in 2017, against estimated non-Patheon Lab Products and Biopharma Services revenue of $7bn, Thermo Fisher realized about $5bn of revenue through its web properties

9 this is not to say that reagents from one vendor can't be used with instruments from another, just that doing so requires some testing and calibration to validate that reagent compatibility with instrument specs

10 I am using the Thermo Fisher's adjusted return on invested capital, which the company defines as "*annual adjusted net income, excluding net interest expense, net of related tax benefit, divided by trailing five quarters' average invested capital*"

11 the cell culture media, single use technologies, chromatography consumables, etc. used by customers to make biologics. This stuff is classified in the Life Sciences segment

12 some cells, like liver cells and ocular cells, can't be removed from and re-introduced back into the body

13 for instance, using high voltage electrical pulses to create temporary pores in the cell membrane (electroporation) and delivering genetic payloads to cells through nanoparticles

14 the list price for Novartis' Kymriah, Gilead's Yescarta, and Spark Therapeutics' Luxturna are $475k, $373k, and $850k, respectively

15 about 80% of gene therapies in the clinic and 70% of gene therapies from preclinical (before human testing) through pre-registration (submitting research plans to a registry) are targeted toward cancer and rare diseases

---

10 Likes

Comments

Write a comment...

© 2023 scuttleblurb · Privacy · Terms · Collection notice
Substack is the home for great writing