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NEWSLETTER

MELIOR INSIGHTS

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Melior
CAPITAL MANAGEMENT

Introduction to Melior Capital Management

MELIOR

/me'ljor/
(from Latin)

BETTER, SOUNDER, SUPERIOR

Melior Capital Management is a Swiss domiciled company introducer and advisory firm focused exclusively on the global life science sector.

We specialise in finding funding for medtech, biotech and pharmaceutical companies by applying institutional quality service and process to raise capital.

Our investment approach is to find qualified innovative projects, with proven management teams, promising data, robust IP, strong corporate governance and a likely opportunity for significant commercial upside in a three to five-year horizon.

In the current environment, many existing companies seeking capital for medical trials have encountered a diminishing supply of funding from governments, private equity firms, investment banks and research foundations in favour of start-ups. At Melior, we combine the global reputation of our scientific, management and advisory members to select best in class investment opportunities with credible upside potential.

Our value proposition is attributable to our world class team and their proven track record in the life-science sector, plus the strong emphasis that we place upon due diligence and first-hand experience. Our goal is to offer attractive and diverse investments to both high net worth private clients and larger corporates through their professional advisers. For our business to be truly successful, we consider the needs of all parties, including our investees, investors and professional advisers at introduction and throughout the life of the investment. Our financial success depends on funds raised and the financial return of our investees as we share a common goal.

Melior does not accept enquiries from members of the general public, but we welcome enquiries from professional intermediaries.

Melior Capital Management

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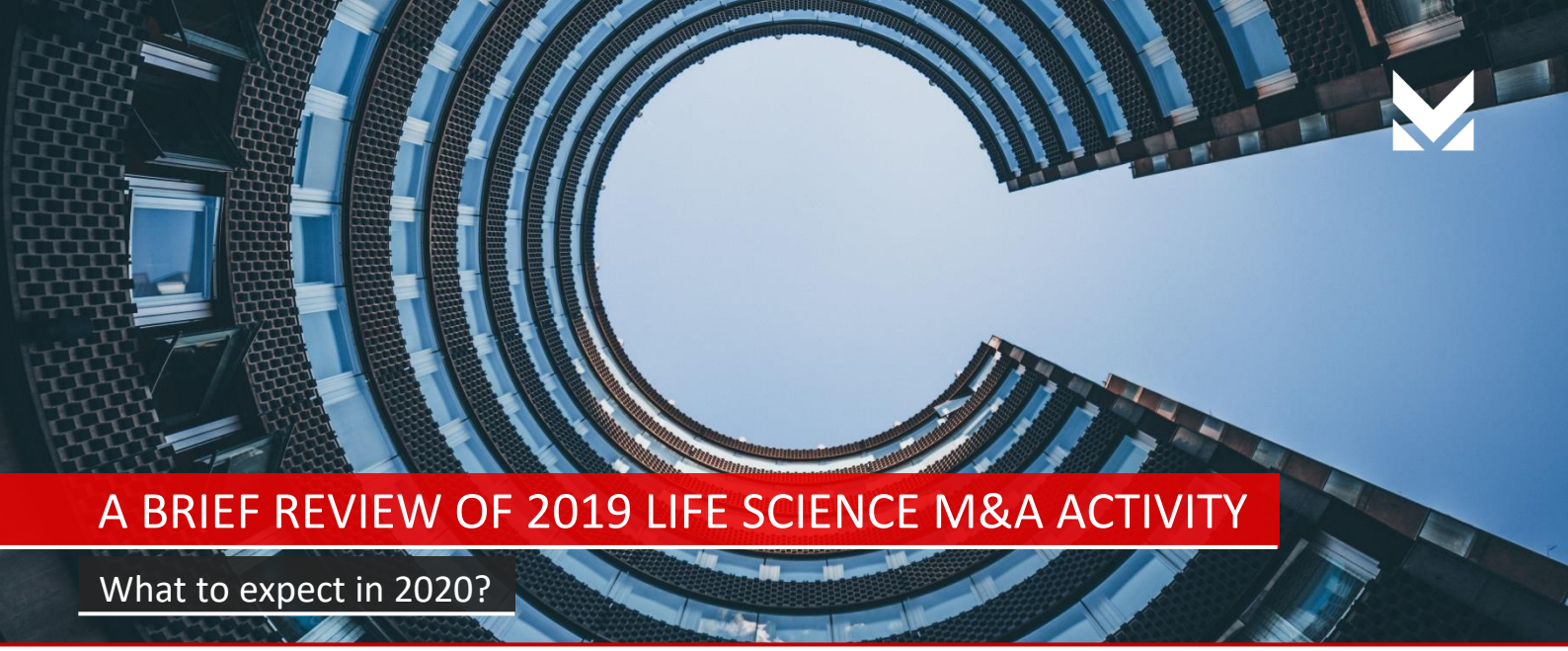


A BRIEF REVIEW OF 2019 LIFE SCIENCE M&A ACTIVITY

What to expect in 2020?

For life science merger & acquisitions, 2019 reached an all-time record with deals totalling $358.5bn, which surpassed the previous high of 2014. Compared to 2018, there was a 62% increase in deal value, although the number of deals remained at the same level as 2019 at 248. The life science sector saw 12 megadeals in 2019, summarised below.

Date	Target	Acquirer	Value ($bn)	Sector
03 Jan	Celgene	Bristol-Myers Squibb	99.5	Biotech
25 Jun	Allergan	AbbVie	86.0	Pharma
25 Feb	GE – BioPharma	Danaher	21.4	Other
26 Aug	Otezla (Celgene)	Amgen	13.4	Biotech
17 Jun	Array BioPharma	Pfizer	11.5	Biotech
24 Nov	The Medicines Company	Novartis	9.6	Biotech
07 Jan	Loxo Oncology	Eli Lilly	8.0	Biotech
20 Aug	Bayer Animal Health	Elanco Animal Health	7.6	Pharma
02 May	Acelity	3M	6.7	Medtech
08 May	Xiidra (Shire)	Novartis	5.3	Pharma
04 Nov	Writght Medical	Stryker	5.3	Medtech
25 Feb	Spark Therapeutics	Roche	4.9	Biotech

The leading region for 2019 was the US with 65% of total deal value, or $233.9bn, largely driven by the $99.5bn Celgene megadeal. Western Europe kept in-line with its 2018 level at $105.7bn or 30%, a figure dominated by the $86bn Allergan acquisition. Interestingly, deal number-wise, Europe only accounts for 13%, which denotes that the European average deal size is higher than global levels, a trend that continues from 2018. Asia Pacific totalled $7.7bn or 2% in 2019, while the Rest of the World was $11.2bn or 3%, both being at a level lower than usual.

According to Ernst & Young (EY), in the first half of 2019, big pharma companies spent 39% of their capital on R&D, 39% on share buybacks, 13% on dividends and only 9% on M&A. This behaviour creates short-term shareholder benefits, but puts pressure on future revenues, as a significant amount of capital is not reinvested in new projects. At the same time, this serves as a great opportunity for smaller-sized, nimble and innovative life science projects, which have a greater level of flexibility, narrow-focus and more efficiency in developing future life science blockbusters. We seek these investee opportunities.

EY forecasts that the level of life science M&A deals will continue to be active in 2020, but it is "highly unlikely" that it will pass the 2019 high. EY predicts that the big medtech and biotech companies will be more active in 2020.

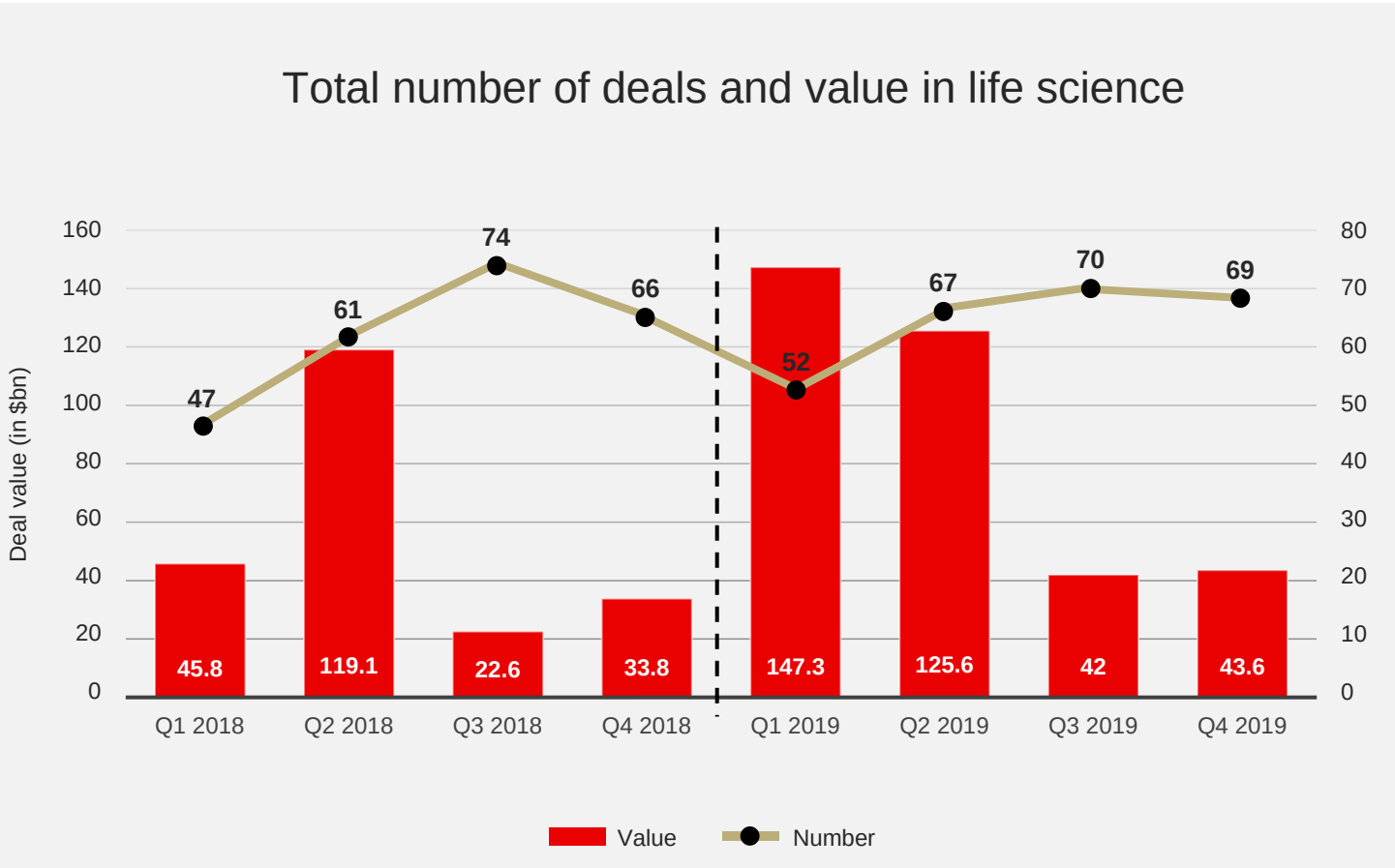
The financial capacity of the life science sector to pursue acquisitions is currently estimated at $1.4tn. One-third of the big pharma companies are able to pursue deals north of $40bn, although companies like Merck&Co, Novartis and Roche seem to be uninterested in such deals. Takeda, AbbVie and Bayer rank among companies with least

firepower for 2020, the first two having recently spent $60+bn on buyouts. Johnson & Johnson, Novo Nordisk, Pfizer, AstraZeneca and Eli Lilly are among big pharma companies capable of large deals this year.

An emerging concept in the life science industry are the digital technologies, where the life science companies prefer partnerships, for example, Novartis and Microsoft, Gilead Sciences and Glympse Bio, rather than to acquire capabilities into data analysis and artificial intelligence, which could immensely benefit areas such as clinical efficiency, patient outcomes and cost measurement.

The growing dynamism of the markets and deep pockets of big pharma represents an opportunity for small emerging innovative companies in the life science sector. Expanding research, decreasing costs and increasing efficiencies offer an opportunity for life science start-ups, but also for investors looking for significant returns. According to Kempen's Life Sciences Investor Survey, there is +107% increase in interest for Phase I assets, thus attracting investors that are ready to assume a higher risk and seeking a higher potential return.

Sources: *PWC, EY, Melior Insights Team*



BIG PHARMA'S PURSUIT OF NEW REVENUE STREAMS

The case study of Eli Lilly

Big Pharma companies are competing for the most innovative assets on the market to maintain their market position and to fuel their growth. A company that spends $5.6bn on R&D yearly, still invested $12.2bn (not adjusted for inflation) in the last 3 years to purchase 5 companies and announced their intention to purchase another 3 companies for a cost of between $1bn and $5bn each, during 2020.

Recently, the CFO of Eli Lilly, Josh Smiley, announced that they are planning to purchase a company per quarter in 2020, worth between $1bn and $5bn, focusing on clinical or late pre-clinical drugs, around the three major therapeutic areas of Lilly, which include oncology, immunology and diabetes.

COMPANY PROFILE

- Founded on May 10, 1876
- HQ located in Indianapolis, Indiana, U.S.A.
- 33,000 employees worldwide, 7,800+ of which are engaged in R&D
- Clinical research conducted in more than 55 countries, R&D facilities in 8 countries
- Manufacturing plants located in 8 countries; products marketed in 120 countries
- 2019 results:
  - $22.3bn - net sales
  - $8.3bn - net income
  - $8.89 EPS
  - $2.58 dividends per share
- R&D expenditures
  - $5.6bn / year or
  - $21.5m / workday
- R&D, as % of sales - 25.1%
- Percentage of total workforce - 23%
- Average cost to discover and develop a new drug: $2.6 billion

2020 Dermira

In Jan 2020, Lilly paid $1.1bn for the skin disease company Dermira, including its Phase 3 trial drug inhibiting IL-13 for atopic dermatitis, the US market of which is estimated at $15bn by 2025.

2019 LOXO ONCOLOGY

In Jan 2019, Eli Lilly acquired Loxo Oncology for $8 bn, at a 68% premium, a company that was valued at $200m at its IPO in 2014. Lilly made this acquisition to diversify the oncology-related income of its best-selling cancer drug Alimta, ahead of the expiry of one of its key patents in May 2022.

2018

In May 2018, Lilly acquired 2 companies - Armo BioScience for $1.6bn and AurKa Pharma for $575m. Armo has developed a Phase 3 immuno-oncology drug which has shown clinical benefit as a single agent and in combination with chemotherapy as well as other immunotherapies. AurKa is working on a solid tumour inhibitor, originally discovered by Lilly and then sold to a Life Science focused venture capital firm, which established AurKa, oversaw its development and then sold back to Lilly.

2017

In Jan 2017, Lilly announced the purchase of CoLucid Pharmaceuticals for $960m. This transaction enhanced the company's existing portfolio in pain management for migraines. Interestingly, Lasmiditan, the main object of the deal, was discovered at Lilly and out-licensed to CoLucid in 2005, which then proceeded to decrease the drug risk's related to development and commercialisation.

Sources: *Eli Lilly, BioPharmaDive, TVM Life Science, PR News Wire, Melior Insights Team*

Image: Lilly Around the World

FDA'S NEW DRUG APPLICATIONS APPROVED LIST

What is the focus of pharma companies?

Regulatory approval requires strategy. There are industry experts able to optimally navigate products to approval / clearance by taking advantage of expedited reviews, finding precedents, selecting the best indication for use, identifying ideal populations, picking appropriate outcomes and optimizing study designs. Melior was co-founded by experts who can provide such advice. Our team members have completed more than 70 approvals / clearances during their careers and bring a deep understanding of the underlying science. This expertise is essential when facing life science regulators like the Food and Drug Administration (FDA), European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA).

The prerogative of these agencies to approve drugs, determines the activities of life science companies and the list of approved drugs is an indication of the areas of primary focus, as well as signs of who are the most successful players, and estimates of future cashflows. This article will review the list of New Drug Applications (NDA) approved by the FDA in Q4 of 2019. Commencing in 1938, every drug and class 3 device in the US has to receive FDA approval.

The goals of the NDA are to provide enough information to permit the FDA reviewer to reach the following key decisions:

- Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.
- Whether the drug's proposed labelling (package insert) is appropriate, and what it should contain.
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality and purity.

In Q4 2019, 44 applications were approved, 16 of which were New Molecular Entities (NMEs) and 7 Biologics License Applications (BLAs).

The 44 drugs were divided into 13 different dosage forms – 25% solution, 20% tablets, 18% injectable, 11% capsule, 7% powder and the remaining 19% spread across the aerosol, cream, film, gas, foam, implant, lotion and subcutaneous systems.

Submission classification	Number of NDAs
Type 1- new molecular entity	16
Type 2 - new active ingredient	2*
Type 3 - new dosage form	6*
Type 4- new combination	1
Type 5 - new formulation or new manufacturer	8
Type 7 -drug already marketed without approved NOA	1
BLA	7
Information not available	4

*one of the approved drugs qualified simultaneously for Type 2 and type 4 submission

Submission classification	Drug name	Active ingredients	Company	Type of dosage form/route	Comments
Type 1- new molecular entity	Trikafta (copackaged)	Elexacaftor, ivacaftor, tezacaftor	Vertex Pharmaceuticals	Tablet; oral	Triple combination for treatment of cystic fibrosis in patients ages 12 years and older
	Aklief	Trifarotene	Galderma R&D	Cream; topical	New topical retinoid for treatment of acne
	Scenesse	Afamelanotide	Clivunel Inc.	Implant; subcutaneous	For prevention of phototoxicity in erythropoietic protoporphyria
	Fluorodopa f18	Fluorodopa f-18	Feinstein	Solution; Intravenous	A 505(b)(2) submission for the use as a radioactive diagnostic agent
	Reyvow	Lasmiditan succlnate	Eli Lilly	Tablet; oral	First serotonin 1fagonist for the acute treatment for migraine
	Exem foam kit	Air polymer-type a	Giskit	Foam; Intrauterine	an intrauterine foam used as an ultrasound contrastagent
	Fetroja	Cefiderocol sulfate tosylate	Shionogi Inc.	Powder; Intravenous	Additional treatment option for patients with cUTls
	Brukinsa	Zanubrutinib	Beigene	Capsule; oral	First BeiGene-discovered product approved
	Givlaari	Givosiran sodium	Alnylam Pharmaceuticals	Solution; subcutaneous	Subcutaneous injection for the treatment of adults with acute hepatic porphyria
	Xcopri	Cenobamate	SK Life Sciences Inc.	Tablet; oral	Treatment of partial-onset seizures
	Vyondys 53	Golodirsen	Sarepta Therapeutics Inc.	Solution; Intravenous	Exon skipping RNA therapy for Duchenne Muscular Dystrophy
	Caplyta	Lumateperone tosylate	Intra-Cellular	Capsule; oral	For treatment of schizophrenia
	Tlssueblue	Brilliant blue g	Dutch Ophthalmic	Solution; ophthalmic	first FDA approved dye for use as an aid in ophthalmic surgery by selectively staining the internal limiting membrane
	Dayvlgo	Lemborexant	Eisai Inc.	Tablet; oral	For treatment of Insomnia in adult patients
	Ubrelvy	Ubrogepant	Allergan	Tablet; oral	To treat acute migraine with or without aura in adults
	Oxbryta	Voxelotor	Global Blood Therapeutics	Tablet; oral	First approved treatment that directly inhibits sickle hemoglobin polymerization
Type 2 - new active ingredient	Vumerity	Diroximel fumarate	Biogen	Delayed release capsule; oral	Novel oral fumarate for the treatment of relapsing forms of multiple sclerosis
Type 2 and type 3	Conjupri	Levamlodipine maleate	CSPC Pharmaceutical Group Limited	Tablet; oral	First NDA ever submitted to the FDA by a Chinese pharmaceutical company
Type 3 - new dosage form	Exservan	Riluzole	Aquestive Therapeutics	Film; oral	Early-action approval for the treatment of amyotrophic lateral sclerosis
	Quzyttir	Cetirizine hydrochloride	JDP	Solution; Intravenous	First intravenous formulation of cetirizine
	Secuado	Asenapine	Hisamitsu	System; transdermal	First-and-only transdermal patch for the treatment of schizophrenia
	Amzeeq	Minocycline hydrochloride	FoamIx	Aerosol (foam); topical	First topical minocycline to be approved by the FDA for any condition
	Ibrance	Palbociclib	Pfizer Inc.	Tablet; oral	Approved for the treatment of advanced or metastatic breast cancer
Type 4- new combination	Talicla	Amoxicillin; omeprazole magnesium; rifabutin	Redhill	Delayed release capsule; oral	Only rifabutin-based therapy approved for the treatment of H.pylori infection

Submission classification	Drug name	Active ingredients	Company	Type of dosage form/route	Comments
Type 5 - new formulation or new manufacturer	Bortezomlb	Bortezomlb	Dr.Reddy's Laboratories ltd.	Powder; Intravenous	A 505(b}(2) submission for IV formulation
	Bonsity	Teriparatide	Alvogen	Solution; subcutaneous	Submitted under the 505(b)(2) regulatory pathway
	Biorphen	Phenylephrlne hydrochloride	Eton Pharmaceuticals	Solution; Intravenous	First and only FDA-approved ready-to-use injection for hypotension during anesthesia
	Cabazitaxel	Cabazitaxel	Fresenius Kabl USA	Injectable; Injection	Tentatively approved
	Potassium phosphates	Potassium phosphate, dibaslc and monobaslc	Fresenius Kabl USA	Solution; Intravenous	Submitted under 505(b)(2) application for use as a source of phosphorus
	Reditrex	Methotrexate	Cumberland Pharmaceuticals	Solution; subcutaneous	Treatment of Rheumatoid arthritis, juvenile idiopathic arthritis, and psoriasis
	Nouress	Cysteine hydrochloride	Avadel legacy	Solution; Intravenous	For neonatal patients requiring total parenteral nutrition
	Genosyl	Nitric oxide	Vero Biotech	Gas; Inhalation	First and only FDA approved tankless delivery system for inhaled nitric oxide
Type 7 -drug already marketed without approved NOA	Epinephrine (copackaged)	Epinephrine	Hospira Inc.	Solution; Intravenous	Submitted under 505(b)(2) application for hypotension associated with septic shock
BLA	Zlextenzo	Pegfigrastim-bmez	Sandoz Inc.	Injectable; Injection	Biosimilar to Neulasta
	Reblozyl	Luspatercept-aamt	Celgene Corp.	Powder; subcutaneous	First-in-class erythroid maturation agent (ema) for the treatment of anemia
	Abrilada	Adalimumab-afzb	Pfizer Inc.	Injectable; Injection	Biosimilar to Humira
	Adakveo	Crizanilzumab-tmca	Novartis	Injectable; Injection	First FDA-approved medicine in sickle cell disease
	Beovu	Brolucizumab-dbil	Novartis	Injectable; intravitreal'	First FDA-approved anti-VEGF for the treatment of AMD
	Padcev	Enfortumab vedotin-ejfv	Astellas	Injectable; Injection	First FDA approved treatment in the USA for treatmentof adult patients with locally advanced or metastatic urothelial cancer
	Enhertu	Fam-trastuzumab deruxtecan-nxkl	Daiichi Sankyo	Injectable; Injection	To treat metastatic breast cancer
Not available	Avsola	Infliximab-axxq	Amgen Inc.	Injectable; Injection	Fourth biosimilar to Infliximab
	Arazlo	Tazarotene	Bausch	Lotion; topical	First tazarotene acne treatment as a lotion
	Hemady	Dexamethasone	Dexcel Pharma	Tablet; oral	A 505(b){2} submission for treatment of multiple myeloma
	Absorlca Id	Isotretlnoln	Sun Pharmaceuticals	Capsule; oral	Treatment of severe recalcitrant nodular acne in patients 12 years and older

Sources: *PharmaOutsourcing, FDA, Melior Insights Team*

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MELIOR CAPITAL MANAGEMENT:
PIONEERING LIFE SCIENCE INVESTMENT

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III. Members of the Melior Scientific Team have worked on and taken to market a large number of life science projects during their careers, which spans over the past forty years. Some projects added additional revenue streams to an existing big pharma patent portfolio, some were trade-sales and some were IPOs.