



Pharma Partnering Trends Revealed: 2019 Edition

Comprehensive report and expert insight on partnering activity as seen at BIO-Europe®



Introduction

Imagine the hum of hundreds of voices in conversation, pitching, collaborating, and negotiating. Then a bell chimes and those dealmakers emerge from 700 partnering booths and regroup in a dynamic quest for new opportunities and innovations. During this three-day partnering dance, assets are acquired, mergers are made, strategies are mapped, and funding is found. Which therapeutic areas garner the most attention? What are the implications of these meetings for therapies, treatments, and cures? Whose negotiations will result in an important strategic partnership?

Last year, BIO-Europe attendees sent nearly 124,000 requests which resulted in over 26,000 meetings. This included negotiations between biotech and pharma, meetings between private and public companies, and first contacts between emerging startups and potential partners. Since

the most common company pairings, most sought after therapies, and most lucrative assets change every year, this report will provide an aggregate view of developing trends.

This partnering analysis spans the years 2012–2018. We first looked at this data in-depth four years ago in a multi-year examination of event data from 2012–2015, or, one hundred thousand meetings. Three years ago we added data from 2016, then 2017, and this year's report adds 2018 data to that aggregate, reanalyzing the types of alliances, the scope of dealmaking activity, and myriad opportunities that continue to drive drug development at each BIO-Europe international partnering event.

Anna Chrisman

Group Managing Director EBD Group

The past year has certainly made for interesting observation of the biopharmaceutical industry, featuring extensive industry consolidation among Big Pharma, transformative potential of cell and gene therapies, escalation of the artificial intelligence arms race and ongoing rumblings of pricing reform in the US. In such times, it can be tempting to look inwards for security and stability, although this dismisses the myriad opportunities that such disruption offers. Companies that are at the forefront of these dynamic trends are best-placed to succeed, and those that aren't can look to partnering as a means to balance risk with reward.

This analysis represents the fourth tie-up between Pharma Intelligence and EBD Group, sharing insights across Medtrack, Strategic Transactions and anonymized meeting data from BIO-Europe 2018, to delve into the latest partnering trends.

Much like collaborations between our colleagues in the industry, the combined expertise and datasets come together to provide a richer purpose. Partnering remains an essential part of doing business, and this report demonstrates that across all stages of the journey – from identifying opportunities, to conducting meetings, and executing these deals – that activity is reaching an all-time high for the industry.

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Profile of an Opportunity: A Company Perspective – 2019 Update

The prolific M&A activity in pharma/biotech so far this year may portend a shift in the business models of some players in the industry. But as we seek to identify new opportunities in this updated version of "Pharma Partnering Trends Revealed", we find collaborative drug development is still prevalent despite the flurry of company acquisitions.

Whether the goal is to gain access to innovative technologies or expand into new markets, partnering is an effective method for growing pipelines without bearing the entire discovery and development costs. The model works well for larger, well-established companies but is also beneficial for smaller companies without the funds to advance their programs forward. It remains clear that alliances continue to drive drug development for public and private companies alike [Figure 1]. In fact, the marginal decline in partnered portfolios among private companies was offset by a slight increase in proportion of public companies' partnered assets from last year's analysis.

Figure 1. Partnered Drug Portfolios



Source: Medtrack 2019

As collaboration continues to drive drug development, we once again analyzed the current unpartnered pipelines of both sectors across the globe to uncover potential prospects and identify new trends that may be emerging.

Unpartnered pipelines

We reviewed the landscapes of the unpartnered pipelines of both public and private companies at the end of O2 2019 and compared the findings with what was found at the same point in 2018. Except for volumes, little has changed among the two groups in how unpartnered drugs are distributed by phase [Figures 2 and 3]. The number increased by roughly 20% at the preclinical phase for both company types. As we've seen in previous years, partnering opportunities are most abundant when compounds are at the very early stages of development and diminish considerably once drugs enter the clinic. The trend clearly reflects the investment cycle of drug development. Licensing a drug during discovery and preclinical testing typically warrants lower upfront and milestone

payments than those that advanced to later-stage trials. This is most evident with private companies as they experience a more drastic decline in unpartnered assets between preclinical and Phase I than their publicly-traded counterparts. By Phase III, relatively few opportunities for collaboration remain with either company type, but our current analysis shows a slight uptick in the number of unpartnered assets at this stage with the public sector. Based on the success of previous trials, companies often choose to go it alone by Phase III due to the decreased risk and greater potential for return on investment. Though Phase III candidates are valued at a premium, garnering higher royalty rates and upfront payments, they are still appealing prospects for collaboration because of the increased likelihood for financial success.

5000

4000

3000

1000

Research Preclinical Phase II Phase III Phase III

2018 2019

Figure 2. Opportunity Distribution by Phase - Public Companies

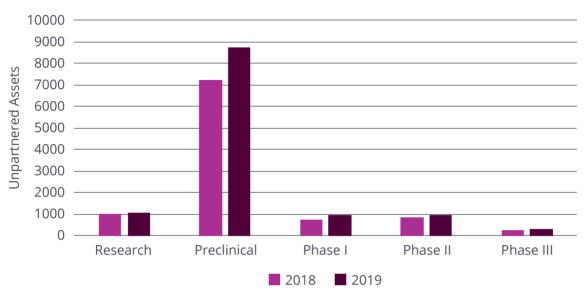


Figure 3. Opportunity Distribution by Phase – Private Companies

Source: Medtrack 2019

Despite the similar distribution of unpartnered assets, identifying suitable partners among private and public companies requires a distinctive approach. We examined the development pipelines of global private and publicly-traded companies and applied separate strategies to each group to uncover opportunities for collaboration. For purposes of this analysis all products in discovery through Phase III (at their highest phase of development, including branded,

biologics and investigational) were included even if the companies were no longer actively developing the products (active development is defined as any reported product development within the past two years. After two years, the candidates are considered "no development reported" or NDR.) These NDR candidates were included since they could be of considerable value to a new partner/acquirer.

Opportunities among private companies across all therapy areas

Based on the criteria described above, we ranked the top 25 privately held companies by the number of unpartnered products in their respective pipelines [Table 1]. Except for some established companies like Boehringer Ingelheim, the group primarily consists of companies with very early stage unpartnered assets. We also found companies on the list actively looking for partners. Aphios Corporation, which is developing 2 new bryoids - bryostatin-22 and bryostatin-23 - for Alzheimer's disease, HIV-1 latency and multiple sclerosis, is seeking collaborative research partners to propel the programs further. Recursion Pharmaceuticals, which raised \$121 million Series C financing to fund the enhancement of its machine learning-enabled drug discovery platform, intends to advance its

preclinical programs into clinical development over the next 18 months either on its own or with development partners.

Several new companies made it to the list this year offering innovative partnering opportunities. Kymab is developing a pipeline of novel human antibody-based therapies for a broad range of indications and challenging targets. Swiss company Humabs BioMed, with its proprietary discovery platform, has promising development programs that address areas of major unmet medical need, including chronic hepatitis B, respiratory syncytial virus/metapneumovirus (RSV/MPV) infections and congenital Zika virus infections. Treos Bio Limited, specializing in personalized immunotherapy, is developing precision cancer vaccines in a variety of indications.

Table 1. Top 25 Private Companies by Number of Unpartnered Products*

Company Name	Prior Rank **	Country	R	PC	I	II	Ш	Total Unpartnered Products
Cellix Bio Private Limited	3	India		58				58
Boehringer Ingelheim International GmbH	2	Germany	2	12	24	15	4	57
Vichem Chemie Research Ltd	1	Hungary		56				56
Recursion Pharmaceuticals LLC	4	United States		55				55
Reven Pharmaceuticals Inc		United States			33	3		36
Aphios Corporation	9	United States	3	30		1	1	35
Druggability Technologies Holdings Ltd	gies 7 Malta			26	2	6		34

Akeso Biopharma Inc	6	China		28	5			33
BL&H Co Ltd	8	Republic of Korea	33					33
Microbiotix Inc	10	United States	2	30	1			33
Humabs BioMed SA		Switzerland		29	1	1		31
Biocidium Biopharmaceuticals	15	Canada		29	1			30
NAL Pharma	12	Hong Kong Special Administrative Region of China	29			1		30
Pierre Fabre SA	11	France	2	12	5	8	3	30
Sunovion Pharmaceuticals Inc		United States	4	20	3	3		30
NovaLead Pharma Pvt Ltd	13	India		27			1	28
Biomay AG	14	Austria	12	12	2	1		27
Celprogen Inc	17	United States		26				26
Chronos Therapeutics	19	United Kingdom		25	1			26
HEC Pharmaceutical Business		China		14	8	1	2	25
Nerviano Medical Sciences	16	Italy		20	2	3		25
Rottapharm SpA		Italy	2	19	1	2	1	25
SOM Biotech	24	Spain		21	3	1		25
Kymab Limited		United Kingdom		23	1			24
Treos Bio Limited		United Kingdom		23		1		24

^{*}By highest phase of development; total product count includes those products in active development and those with no development reported in the past two years
**Previous rank of companies from 2018 published paper

Opportunities among private companies in oncology

Oncology indications continue to dominate drug development, so we once again ranked the top 25 global private companies by number of unpartnered cancer drugs to uncover opportunities exclusive to this space. As expected, there is overlap with the total dataset (highlighted in Table 2) but additional viable options for collaboration emerge among this cohort.

Some noteworthy companies in this group include KSQ Therapeutics which uses its proprietary CRISPR technology for drug discovery and is advancing a pipeline of tumor- and immunefocused drug candidates for the treatment of
cancer, including targeted therapies, adoptive
cell therapies and immuno-therapies. L.E.A.F.
Pharmaceuticals LLC announced it is seeking
partners to accelerate the R&D of four pre-IND
novel molecules that are designed to disrupt
dysregulated serine-glycine 1-carbon metabolism
in cancer and the immune system after receiving
positive FDA response after pre-IND meetings.
Immuno-oncology company F-star has leveraged
partnerships to strengthen its Modular Antibody
Technology and mAb2 programs and currently
has several IO programs in discovery.

Table 2. Top 25 Private Companies by Number of Unpartnered Oncology Products*

Company Name	Prior Rank**	Country	R	PC	I	П	Ш	Total Unpartnered Products
Vichem Chemie Research Ltd	1	Hungary		36				36
Nerviano Medical Sciences	2	Italy		20	2	3		25
Treos Bio Limited	16	United Kingdom		23		1		24
Akeso Biopharma Inc	3	China		20	3			23
Celprogen Inc	4	United States		23				23
Cancer Research Technology	5	United Kingdom	4	15	2	1		22
Hrain Biotechnology Co Ltd		China		16	4		1	21
Hebei Senlang Biotechnology Co Ltd		China		9	10	1		20
Systlmmune Inc		United States		19				19
Innovative Cellular Therapeutics CO LTD		China	1	13	1	2		17
L.E.A.F. Pharmaceuticals LLC	13	United States		17				17

BL&H Co Ltd	8	Republic of Korea	16					16
Syntab Therapeutics	9	Germany		16				16
KSQ Therapeutics		United States		15				15
Nanjing Sanhome Pharmaceutical Co Ltd	14	China		12	2	1		15
Shanghai De Novo Pharmatech Co Ltd	22	China		13	2			15
Aphios Corporation	17	United States		13			1	14
Beijing Jacobio Pharmaceutical Co Ltd		China		13	1			14
Bio-Thera Solutions Ltd		China		11	2		1	14
Endocyte Inc		United States	2	8	4			14
Icell Kealex Therapeutics	11	United States		14				14
Quimatryx	15	Spain	2	12				14
HitGen Ltd	18	China		12	1			13
iCell Gene Therapeutics		United States	1	9	3			13
F-star Biotechnology Limited		United Kingdom		12				12

^{*}By highest phase of development; total product count includes those products in active development and those with no development reported in the past two years
**Previous rank of companies from 2018 published paper

Public company analysis - all therapy areas

As mentioned previously, different strategic approaches are necessary to identify potential partners based on company type. We re-evaluated the collaborative opportunities with public companies again this year by leveraging burn rates to differentiate companies that may need to raise capital. Companies with promising pipelines but less than two years in cash remaining may consider partnering as an alternative to a pure financing, thus enabling them to pursue development while sharing the overall cost. Table 3 represents the top 25 global public companies with less than two years of cash remaining (as defined by cash on the latest balance sheet/ annual cash burn rate), ranked by total number of unpartnered products across all therapy areas.

Once again Immunomedics, Omeros and Compugen top the list with the largest number of unpartnered drugs in their respective pipelines. Next in line and new to the ranking this year is Sorrento Therapeutics with 34 unpartnered assets and one that has entered the clinic. The company recently raised \$25 million in a public offering and

intends to use the funds to advance its portfolio of immuno-oncology assets including CAR-T cell therapies and bispecific antibodies. But partnering remains a key component of its business strategy. UK biotech Redx Pharma PLC, focused on anticancer and fibrosis targets in areas of unmet need, develops novel compounds using its drug discovery expertise and then advances them in the clinic through partnerships. Several of these candidates are expected to enter Phase I in 2020. Alliances are a key driver in the advancement of Celyad's pipeline, and several of its CAR-T NK cell-based immunotherapies remain unpartnered.

Though most collaborative opportunities presented in this group are at very early phases of development, there are a good number of unpartnered assets that have already moved to the clinic. These programs should not be overlooked as potential investments because companies may be inclined to divest later-stage assets, thus providing greater focus, or share development costs to advance these programs further.

Table 3. Top 25 Public Companies With < Two Years in Cash by Number of Unpartnered Products*

Company Name	Prior Rank**	Country	Years in Cash	R	PC	T	П	Ш	Total Unpartnered Products
Immunomedics Inc	1	United States	1.71	2	38	1	11		52
Omeros Corporation	2	United States	1.06		48		2		51
Compugen Ltd		Israel	0.73		36				36
Novavax Inc		United States	0.77	1	24	2	1		28
Lexicon Pharmaceuticals		United States	1.93		21		4		25

Zosano Pharma	4	United States	0.12		18	5		1	24
Marina Biotech		United States	0.01	1	15	7			23
Celldex Therapeutics		United States	0.7		15	3	1		19
IntelGenx Corp		Canada	0.5	3	9	3	3		18
Pivot Pharmaceuticals Inc		Canada	0.53		17				17
Affimed Therapeutics AG		Germany	1.8	2	14	1			17
ProQR Therapeutics NV		Netherlands	0.87		15		1		16
Lipocine Inc		United States	1.47	2	10	1	3		16
ArQule		United States	1.52		12	4			16
Anavex Life Sciences Corp	5	United States	1.46		14		1		15
Helix BioMedix Inc	7	United States	0.08	2	12				14
Stemline Therapeutics Inc		United States	1.39		14				14
Immuron Ltd		Australia	0.11	3	4	1	4	1	14
Oncobiologics Inc		United States	0.15	1	11				12
Medlab Clinical LTD		Australia	0.19		11		1		12
Onconova Therapeutics Inc		United States	0.35		12				12
Apricus Biosciences Inc	8	United States	0.57	2	9		1		12
KemPharm Inc		United States	0.65		10	1		1	13
Rigel Pharmaceuticals Inc		United States	1.08		11	1			12
Inovio Pharmaceuticals Inc		United States	1.16		6	4	2		12

^{*}By highest phase of development; total product count includes those products in active development and those with no development reported in the past two years

^{**}Previous rank of companies from 2018 published paper

Oncology prospects among public companies

We also re-evaluated the top 25 global publicly traded companies by number of unpartnered oncology assets based on burn-rate as we did with the private companies. Excluding the overlap from the list of companies with pipelines from all therapy areas (highlighted below), additional opportunities for collaboration emerge in the oncology space. In fact, many have publicly announced their willingness to pursue external collaborations to advance their programs.

For example, MacroGenics uses collaborations in its growth strategy to develop pipeline candidates from its proprietary suite of next-generation antibody technologies. Among the candidates it has yet to co-develop is MGC018, an antibodydrug conjugate (ADC) comprising a humanized B7-H3 mAb conjugated to a potent DNA alkylating payload via a cleavable peptide linker. MGC018 is

designed to target solid tumors expressing B7-H3 and is currently being evaluated in a Phase I dose escalation study. Canadian Aptose Biosciences is developing personalized therapies to address unmet medical needs in oncology, with a focus on hematologic malignancies. It has several programs positioned for partnering including APTO-253 which is at the Phase 1b clinical stage for the treatment of patients with relapsed/refractory blood cancers, including AML and highrisk MDS. Cellectar Biosciences is developing new targeted treatments for rare/orphan designated cancers, leveraging its proprietary phospholipid ether (PLE) platform to specifically target treatments for improved efficacy.

Despite these promising programs, limited cash flow may impede development moving forward. Forming an alliance with any of these companies could prove to be a favorable investment.

Table 4. Top 25 Public Companies With < Two Years in Cash by Number of Unpartnered Oncology Products*

Company Name	Prior rank**	Country	Years in Cash	R	PC	ı	П	Ш	Total Unpartnered Products
Immunomedics Inc	1	United States	1.21		37	1	11		49
Sorrento Therapeutics Inc		United States	0.33		23	1			24
ABL Bio		Republic of Korea	1.28		18				18
Avacta Group plc	7	United Kingdom	1.17		18				18
Compugen Ltd	2	Israel	1.23		17				17
PHARMA MAR SA		Spain	0.94	1	11	2	3		17
AEterna Zentaris Inc		United States	0.75		15	2			17

Stemline Therapeutics	4	United States	1.33		15			 15
Aptose Biosciences Inc		Canada	0.62		12	1	1	 14
Omeros Corporation	5	United States	0.39		14			 14
Celldex Therapeutics	12	United States	1.69		10	2		 12
Cellular Biomedicine Group Inc	17	United States	1.13		7	1	4	 12
Anavex Life Sciences Corp	10	United States	0.81		11			 11
Onconova Therapeutics Inc	8	United States	0.45		11			 11
MacroGenics Inc		United States	1.92		8	2		 10
Merrimack Pharmaceuticals Inc		United States	1.76		9	1		 10
Five Prime Therapeutics Inc		United States	1.52		9	1		 10
Advaxis Inc	13	United States	0.99		9		1	 10
Cellectar Biosciences		United States	0.67		9	1		 10
BioLineRx Ltd		Israel	1.77		9			 9
Transgene Biotek Ltd		India	0.02	1	8			 9
Outlook Therapeutics Inc		United States	0	1	8			 9
Inovio Pharmaceuticals Inc	14	United States	1.36		5	2	1	 8
GT BIOPHARMA INC		United States	0		8			 8
Celyad SA		Belgium		7	1			 8

^{*}By highest phase of development; total product count includes those products in active development and those with no development reported in the past two years

^{**}Previous rank of companies from 2018 published paper

Building Relationships at BIO-Europe

Pharma Intelligence examined partnering trends based on meeting activity from BIO-Europe between 2013 and 2018, using data from the partneringONE® database, which was provided by EBD Group. The dataset was limited to companies attending fall BIO-Europe events between 2013 and 2018, with this year's scope expanded to include all industry players and not just those designated as Pharma and Biotechnology – Therapeutics and Diagnostics (Biotech). Where appropriate, historical comparisons have been made with the Pharma and Biotech subset, while the 2018 snapshot includes all company types.

If companies chose to disclose additional metrics, these could include employee number, country, therapeutic area, and products (phase, therapeutic sector, molecule type, and partnering status). Since not all companies provided the same level of detail in their profiles, an element of reporting bias may have an impact on observations derived from the data. As with previous data, all company and product statistics were anonymized, and included the assignment of a different anonymous ID per company each year.

In the following analysis, the meeting requester is designated as the "From company" while the recipient of the meeting request is the "To company." The companies meeting will be referred to as "pairs" or "pairings." A small proportion of meetings (0.2%) included three different parties, and these have been double-counted accordingly to accurately denote the number of inter-company pairings. Unfulfilled meeting requests, such as those that were declined or cancelled, were excluded from the analysis.

An overview of BIO-Europe meeting activity

The partnering booths and rooms of the 2018 BIO-Europe meeting in Copenhagen played host to an impressive 27,310 meetings, as shown in Table 5. These meetings featured 1,959 different attending companies, with each company successfully conducting an average of 13.9 onsite appointments through the course of the three-day conference. The most prolific company packed in a diary-busting 155 different meetings, while 55 companies in total secured more than 50 arrangements.

Table 5. Overview of BIO-Europe meeting activity, 2018

Average # requests per company resulting in meetings	13.9
Total companies requesting meetings	1959
>50	55
41 to 50	33
31 to 40	61
21 to 30	228
11 to 20	583
6 to 10	483
1 to 5	516
# requests resulting in meetings (company count)	
meetings	00
# requests resulting in multiparty	66
# requests to a single company, resulting in meetings	27244
Total # requests resulting in meetings	27310

A like-for-like comparison with previous years' datasets for the Pharma and Biotech subset showed that BIO-Europe 2018 was the busiest yet. Figure 4 reveals 16% and 7% year-on-year increases in the total number of meetings and companies, respectively. The increased volume of interactions was driven not only by a larger

attendance, but also greater engagement as the average requests per company also rose 8% to 11.1 meetings. The increase in total meeting requests in 2018 lies within a similar range to the expansions of 2017 (19%) and 2016 (12%), although the 2013–15 timeframe showed only modest change.

Figure 4. Overview of BIO-Europe meeting activity between Pharma and Biotech, 2013–18



Companies defined as having a biotech focus were the most active with partnering discussions, both in terms of instigating (8,566) and accepting (10,783) meeting requests. Pharma is also heavily represented as established industry players with a wide range of capabilities, especially commercial, that it can offer to potential partners. Providers of specialist services such as consulting and Contract Research Organization (CRO)/Contract Manufacturing Organization (CMO) firms were also among the most active companies at BIO-Europe, and unsurprisingly these sectors carried a strong bias towards setting up meetings, rather than accepting requests from others, as shown in Table 6.

The most common pairing was Biotech to Pharma (B to P), as has been noted across previous years

of BIO-Europe meetings, although 2017 was the slight exception. In this year, Pharma to Pharma (P to P) meetings were the most common, although this reverted back to a more distant fourth place in 2018, marginally behind B to B and P to B interactions. Outside of the traditional pairings, biotech companies were heavily engaged by consulting and CRO/CMO firms. Platforms such as BIO-Europe offer unique opportunity for specialized biotech companies not only to showcase their research to larger partners, but also to gain expertise from other second parties that may fill a particular knowledge or capabilities gap. Consulting and CRO/CMO companies were unable to gain as much traction from Pharma partners, as these companies typically have greater scale and in-house expertise.

Table 6. BIO-Europe meeting activity by sector, 2018

		To company											
	Sector	Biotech	Pharma	CRO/ CMO	Investor	Consulting	Public	Others	Total				
	Biotech	2944	3473	350	752	343	285	419	8566				
	Pharma	2876	2821	278	189	365	266	307	7102				
any	Consulting	1720	1037	361	187	260	172	282	4019				
compa	CRO/CMO	1572	860	468	74	181	140	182	3477				
	Public	396	356	119	84	72	150	89	1266				
From	Investor	539	204	20	165	46	42	61	1077				
	Others	736	504	186	115	112	102	114	1869				
	Total	10783	9255	1782	1566	1379	1157	1454	27376				

Note: The "Consulting" sector refers to companies with "Professional Services and Consulting" in their partneringONE® profile, while "CRO/CMO" refers to those defined as "Biotechnology / R&D Services". The "Others" segment includes the following company types: "Biotechnology - other ", "Media", "Medical Technology, "Not Specified", "Public / Non-Profit Organizations/Institutes" and "Supplier & Engineering".

Table 7 provides an overview of the leading company locations involved in partnering discussions at BIO-Europe 2018, in addition to the number of interactions between these. As in previous years, US-based companies had the largest representation in 2018 and meetings between such companies continue to lead by far. The top five country locations are consistent both in terms of requesting and accepting meetings, providing an established pecking order of the US, UK, Germany, Japan and France.

As well as being part of the most meetings in total, the US was the leading participant in meetings for every single other major ex-US country. This clearly demonstrates the leading presence and demand for capabilities of US companies in the global biopharmaceutical industry, even despite the conference taking place in Copenhagen,

Denmark. Outside of the US, other notable interactions included intra-UK and intra-Germany meetings, as has been noted in previous years. UK companies were particularly active in terms of requesting meetings with other potential European partners, with Brexit an obvious added topic of conversation with BIO-Europe 2018 falling just weeks before the European Union and the UK concluded negotiations on the terms of its withdrawal.

Outside of the top five countries, Switzerland retains its leading presence in the industry, while the Nordic countries were strongly represented by companies in the Netherlands, Denmark and Sweden. South Korea was among the top ten countries requesting partnering discussions, while China featured tenth in the list of countries accepting meetings [Data not shown].

Table 7. Leading country pairings at BIO-Europe 2018 by meeting count

		To company									
Co	untry	United States	United Kingdom	Germany	Japan	France	Others	Total			
	United States	879	463	390	347	295	2083	4457			
>	United Kingdom	655	564	386	197	234	1903	3939			
company	Germany	304	251	438	140	143	1109	2385			
CON	Japan	410	243	228	91	124	1094	2190			
Om	France	241	197	195	139	156	939	1867			
교	Others	2147	1261	1255	878	761	6236	12538			
	Total	4636	2979	2892	1792	1713	13364	27376			

As previously mentioned, a limitation of the dataset is the fact that not all companies provide the same level of detail in their partneringONE® profile, which is the case for employee number. Each year, the largest number of meetings took place between companies where one or both parties did not disclose their employee headcount. Among the companies who did provide this metric, the largest number of meetings were requested by smaller companies (10-50 employees) looking to meet with similarlysized companies, or even those with fewer than 10 employees [Table 8]. This is a change from previous years, in which smaller companies were most active in seeking partnership discussions with the largest companies (>10K), although this deviation likely represents the broadening of the dataset to include non-Pharma and Biotech companies such as consulting and research firms. In general, there is a trend towards the smaller companies instigating more meetings and the larger companies being the secondary participant, consistent with the general concept of the meeting being a forum for smaller biotech companies to partner with larger companies for specific expertise. Indeed, 70% of all the meetings that the >10k companies accepted involved participants with fewer than 100 employees, excluding those without a specified headcount. Despite this year so far seeing several high-profile megamergers such as AbbVie-Allergan, Bristol-Myers Squibb-Celgene, and Takeda-Shire, there were only 85 documented on-site discussions between such >10k employee giants, just 60 of which exclusively involved Pharma or Biotech companies.

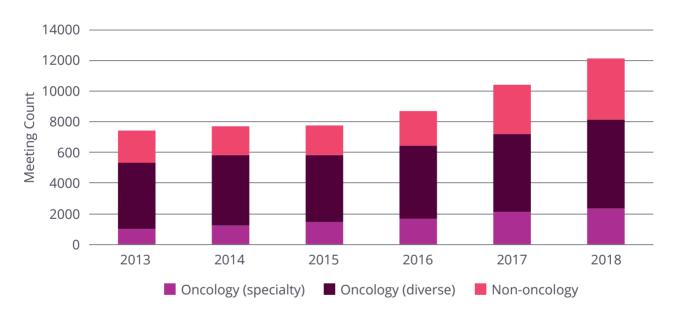
Table 8. Leading company size pairings at BIO-Europe 2018 by meeting count

F.o.	- playes					To con	npany				
	iployee tegory	<10	10-50	51-100	101- 500	501- 1000	1001- 5000	5001- 10K	>10K	N/A	Total
	<10	346	461	171	255	89	196	102	290	1115	3025
	10-50		788	281	464	151	361	163	534	1841	5189
	51-100	202	273	92	148	54	142	68	173	576	1728
any	101-500	347	471	144	265	81	149	60	193	912	2622
omp	501-1000	120	200	62	111	31	61	17	43	353	998
	1001-5000	242	378	115	149	66	128	38	84	637	1837
From	5001-10K	91	142	60	87	22	26	11	28	245	712
_	>10K	220	321	114	143	45	96	33	85	534	1591
	N/A	1119	1639	568	846	246	665	283	863	3445	9674
	Total	3293	4673	1607	2468	785	1824	775	2293	9658	27376

Oncology continues to be the most frequently disclosed therapeutic area (TA) of companies involved in BIO-Europe meetings, as either the requester or the recipient. This large cohort of companies is consistently active at BIO-Europe each year, and approximately 67% of meetings in 2018 included at least one oncology company, excluding company types not involved with drug discovery research. When limiting the dataset to companies who listed oncology as the sole

therapeutic area in their profile (specialty), meeting numbers dropped and comprise approximately 19% of all meetings. These proportions represent a slight and arguably non-meaningful decline over 2017, although is counter-balanced by the increased volume of interactions. In total, the number of meetings between drug discovery companies with at least one oncology interest rose 14% to 8,161.

Figure 5. BIO-Europe meetings, by company's oncology focus (requester and/or recipient company), 2013–18



Note: Specialty refers to companies only listing oncology as a therapeutic area while diverse includes companies listing oncology as one of multiple therapeutic areas. Instances where a specialty company met with a diverse company are captured under "Oncology (specialty)". Dataset limited to Pharma and Biotech companies.

Outside of oncology, the next most commonly disclosed TAs of companies involved in BIO-Europe 2018 partnering discussions were central nervous system (CNS) and endocrine/metabolic diseases. This is consistent with the scientific agenda of the meeting, with separate tracks

on offer for companies to showcase CNS, rare diseases and microbiome research. The numbers presented in Table 9 are for the entire company dataset, including non-Pharma and Biotech players.

Table 9. Top ten therapy areas for BIO-Europe meeting activity, 2018

Therapeutic area		Meeting count				
		То	Both	Either		
Neoplasms / cancer / oncology	9957	11140	4859	16238		
Diseases of the nervous system	7043	8157	2544	12656		
Endocrine, nutritional and metabolic diseases	6683	7227	2068	11842		
Cardiovascular	5464	5764	1290	9938		
Diseases of the blood and blood-forming organs; immune disorders	5131	5638	1127	9642		
Infectious and parasitic diseases	5357	5362	1283	9436		
Respiratory system	4837	5227	1077	8987		
Musculoskeletal system and connective tissue	4742	4922	942	8722		
Skin and subcutaneous tissue	4746	4814	1164	8396		
Digestive system	4008	4019	732	7295		

As previously noted, BIO-Europe affords companies offering R&D or consulting services a broad audience with which to engage. For those companies with a specified focus of "Biotechnology / R&D Services" or "Professional Services and Consulting" in their partneringONE® profile, the number of successful appointments is shown in Table 10, according to their specified service capabilities. Companies providing CRO capabilities were most in-demand, both in terms of arranging and accepting meetings in 2018. Despite there being much discussion of

demand for advanced drugs such as gene and cell therapies being outstripped by manufacturing capacity, companies offering a CMO service only ranked ninth in the list of providers. As advanced therapies enter mainstream clinical practice for more prevalent disorders such as hemophilia, this portion of the R&D services market will certainly burgeon. Many of the other service capabilities most in demand were those of the "Professional Services and Consulting" companies, such as business development, due diligence, management consulting and deal arranging.

Table 10. Top ten service capabilities for BIO-Europe meeting activity, 2018

Comice comphility	Meeting count				
Service capability	From	То	Both	Either	
CRO (Contract Research Organization)	2350	1046	211	3185	
Business development	2070	654	46	2678	
Due diligence	1260	575	13	1822	
Management consulting	1365	404	13	1756	
Deal arranger	1287	485	18	1754	
Analytical services	1170	575	46	1699	
Other	1157	488	41	1604	
Valuation	1172	421	10	1583	
CMO (Contract Manufacturing Organization)	896	516	59	1353	
Technology transfer	851	466	17	1300	

Partnership Deals Update (H2 2018-H1 2019)

Within the biopharma industry, we analyzed all worldwide partnership deals from H2 2018 through H1 2019 that included the licensing of drug compounds in the research through postmarketing phases (excluding alliances involving trial collaborations that do not explicitly state licensing). We also took a closer look at the top ten deals in the space. The overall data demonstrated notable trends across therapy areas, payment structures, and phase distribution. In the following section, please note that deal value is defined as the sum of disclosed upfront payment(s) plus any announced or received milestone payments.

After a rather disappointing Q2 2018 – with 280 partnership deals (valued together at \$11.4bn; see prior report) marking a significant decline from the robust deal activity and high dollar values seen in Q1 2018 and Q4 2017 – Q3 2018, the opening

quarter of our review period, more than doubled to \$25.6bn across 311 deals. The numbers then steadily rose to a high of 356 deals in Q1 2019, which not only had the most deals, but also the greatest aggregate dollar volume (\$44.0bn), which can be attributed to thirteen, billion-dollar-plus transactions completed during that quarter. But then, similar to last year's pattern, deal activity experienced a sharp drop off in Q2 2019, which had 280 deals (valued at \$21.3bn) [Figure 6].

In all, the number of partnership deals over the current review period (1,293) is comparable to the 1,283 deals (with an aggregate value of \$86.8bn) completed in the prior time frame, yet the current total potential deal value, at \$129.1bn, showed a 49% increase from the previous review period [Figure 6].



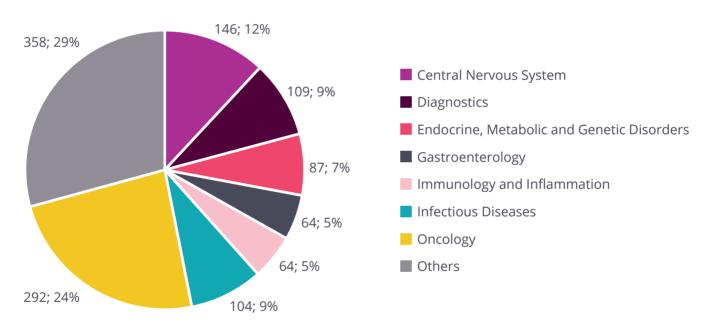
Figure 6. Total deal volume and value distributions, H2 2018-H1 2019

Oncology remains on top; CNS follows

Examining data by therapy area, we see once again that oncology deals remain in the top spot both by number of deals and total deal value. Oncology represented 24% of total volume (on par with our prior analysis), and in terms of total deal value, it held an impressive 41% of the aggregate [Figures 7, 8]. Also in line with prior analysis, deal activity in the CNS space came in second, accounting for 12% of the total deal activity and 12% of the top transactions by deal value.

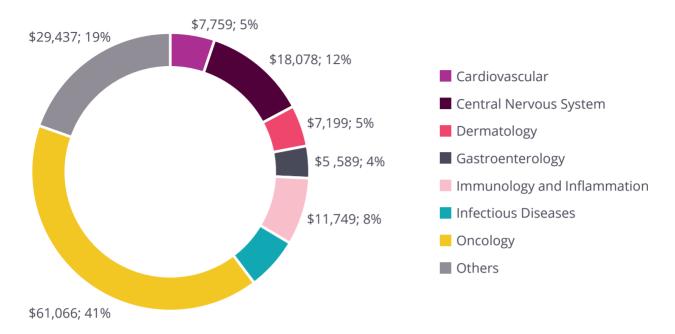
A closer look at the top oncology deals shows a continued strong interest in immuno-oncology and combination cancer therapies. The top deal by dollar volume – AstraZeneca PLC's co-development and co-commercialization collaboration with Daiichi Sankyo surrounding the antibody-drug conjugate (Fam-) trastuzumab deruxtecan (DS-8201) – could top \$6.9bn in value, comprising a \$1.35bn up-front payment by AZ (the firm's largest ever) and \$5.5bn in additional payments.

Figure 7. Partnership deals total volume by therapy area, H2 2018–H1 2019



^{*}Others includes other therapy areas and selected medical device and diagnostics deals.





^{*}Others includes other therapy areas and selected medical device and diagnostics deals.

Milestones again account for most of deal values

As seen in the last review period, those alliances including an announced milestone component continue to dominate over up-front payments in deal structures. During H2 2018–H1 2019, this portion of partnerships accounted on average for 56% of the total potential deal values [Figure 9]. Notably, in Q3 2018, milestones made up 71%

of the aggregate; likely due to five deals with billion-dollar-plus potential future payments, led by Affimed's August 2018 innate cell antibody engager partnership with Genentech, in which Affimed stands to get up to \$5bn in milestones (\$250mm in development; \$1.1bn for regulatory; and \$3.6bn related to commercialization) should it meet certain goals.

50,000 45,000 Total Deal Value (USD mm) 40,000 35,000 30,000 25,000 20,000 15,000 10,000 5,000 0 Q3 2018 Q4 2018 Q1 2019 Q2 2019 ■ Total Deal Value ■ Upfront ■ Milestones

Figure 9. Partnership deal breakdown by payment type, H2 2018-H1 2019

Large deals figure prominently

The top ten licensing deals – by total deal value (including all potential realized and unrealized development and commercial milestones) – together accounted for 31% of the total deal value during H2 2018 to H1 2019 [Table 11]. This group has a heavy cancer focus, with six partnerships including one or more oncology asset. AstraZeneca (AZ) completed two large deals in the top-ten group (together worth \$9.3bn): one,

the aforementioned tie-up with Daiichi Sankyo for HER2-expressing cancers, and a reverse-licensing deal in which AZ sold Swedish Orphan Biovitrum exclusive rights to commercialize the respiratory syncytial virus therapy Synagis (palivizumab) in the US for \$1bn up front. Overall, during this review period AZ was involved in 20 alliances, predominantly in oncology, but across a variety of therapeutic areas.

Table 11. Top partnership deals by total deal value, H2 2018–H1 2019

Deal Date	Licenser	Licensee	Products/Technologies	Deal Value (USD mm)	Broader Therapeutic Area	Royalty
3/28/2019	Daiichi Sankyo Co. Ltd.	AstraZeneca PLC*	Antibody-drug conjugate DS-8201 (trastuzumab deruxtecan) for HER2- expressing cancers, including breast and gastric, and non-small cell lung and colon cancers	6,900	Oncology	Partners share all profits on global sales of DS-8201
5/8/2019	Takeda Pharmaceutical Co. Ltd.	Novartis AG	Xiidra (lifitegrast; SAR- 1118), a lymphocyte function-associated molecule inhibitor topical solution for dry eye	5,300	Ophthalmic	N/A
8/24/2018	Affimed NV; Genentech Inc.	Affimed NV; Genentech Inc.	Innate immune cell natural killer (NK) cell and T-cellimmunotherapies against certain Genentech-selected targets for various solid and hematological tumors using Affimed's Redirected Optimized Cell Killing (ROCK) platform; Affimed also non exclusively licensed Genentech IP to help in R&D	5,046	Oncology	Undisclosed royalty rate
2/5/2019	Merck KGaA	GlaxoSmithKline PLC; Merck KGaA*	Cancer immunotherapy M7824 (bintrafusp), a bifunctional fusion protein for cancers including non- small cell lung	4,234	Oncology	The companies will share costs and profits equally

2/28/2019	Abpro	Nanjing Chia Tai Tianqing Pharmaceutical Co. Ltd.	Discover and develop bispecific antibodies in immuno-oncology, including T-cell engagers, using Abpro's DiversImmune discovery platform	4,000	Oncology	Undisclosed royalty rate
10/31/2018	Arrowhead Pharmaceuticals Inc.	Janssen Pharmaceuticals Inc.	ARO-HBV, a third-generation subcutaneously administered RNAi therapy for chronic hepatitis B and up to three targets outside of Arrowhead's current pipeline; Arrowhead's Targeted RNAi Molecule (TRIM) platform	3,750	Infectious Diseases	Royalties up to the mid- teens
12/19/2018	Dicerna Pharmaceuticals Inc.	Eli Lilly & Co.	Dicerna's GalXC technology to discover and develop RNAi therapies for cardio- metabolic diseases, neurodegeneration, and pain	3,705	Cardiovascular; Central Nervous System; Metabolic	Mid-single to low-double- digit royalties
7/12/2018	Immatics Biotechnologies GmbH	Genmab AS	Next-generation bispecific immunotherapies for cancer; Immatics' XPRESIDENT high-throughput peptide detection platform and T-cell receptor technology to discover tumor targets	2,804	Oncology	Undisclosed tiered royalties
6/19/2019	Nurix Inc.	Gilead Sciences Inc.*	Targeted protein degradation treatments for cancer and other diseases; Nurix's discovery platform to identify agents that use E3 ligases to induce targeted protein degradation of certain targets. Gilead has the option to license up to five targets, while Nurix retains an option to codevelop and co-detail up to two in the US	2,345	Oncology	Up to low- double digit royalties
1/24/19	AstraZeneca PLC	Swedish Orphan Biovitrum AB	Synagis (palivizumab; MEDI493) respiratory syncytial virus (RSV) vaccine; MEDI8897 antibody candidate for RSV	2,315	Infectious Diseases; Respiratory	Sobi participates in AZ's share of profits and losses related to RSV therapy MEDI8897

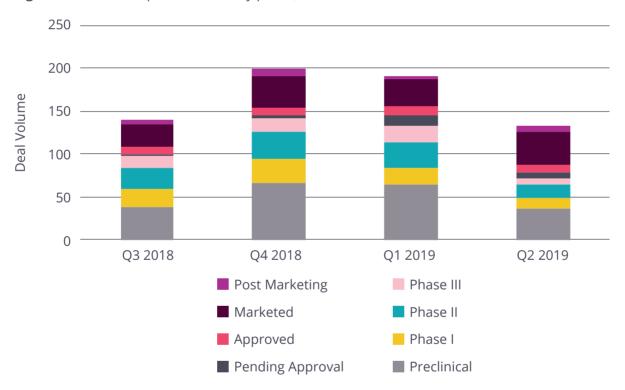
Source: Medtrack; Strategic Transactions 2019

Preclinical deals lead other phases

Looking at partnerships by development stage at time of signing (from preclinical through postmarketed; Phase IV additional trials and research-stage deals were excluded from this analysis) shows that alliances with at least one asset in the preclinical phase were both the most popular in terms of deal volume, making up 31% of all deals,

and at \$51.1bn, also attracted almost half the aggregate dollars of the current review period [Figures 10, 11]. Q1 2019 shows high dollar values for both Phase III and Phase II assets mostly due to outlier transactions during that quarter by AZ/ Daiichi (\$6.9bn) and GlaxoSmithKline/Merck KGaA (\$4.2bn), respectively.

Figure 10. Partnership deal volume by phase, H2 2018-H1 2019



Preclinical

Phase II

Phase III

Pending Approval

Approved

Marketed

Post Marketing

0 2000 4000 6000 8000 10000 12000 14000 16000 18000 20000 22000 24000

Deal Value (USD mm)

■ Q2 2019 ■ Q1 2019 ■ Q4 2018

Figure 11. Partnership deal value by phase, H2 2018–H1 2019

Source: Medtrack 2019

Q3 2018

Royalties remain a key dealmaking component

Examining the average distribution of disclosed royalties across phase at deal signing, a popular trend emerges vet again (as seen in the previous review period; see prior report). Partnerships including an asset at a later phase typically garner the highest royalty, while deals including preclinical assets tend to bring in lower royalties [Figure 12]. Phase II and Phase III deals (at 17.9% and 17.2% average royalties, respectively), both beat out partnerships involving a marketed product, where the average royalty rate was 16.9%. Preclinical-stage deals had the lowest average royalty at 9.7%, but this figure is higher than the 7.8% of the previous review period. In fact, the current analysis also shows an uptick in the royalty rates for all phases – particularly Phase II, which went from 11.7% to 17.9% – with the exception of approved products (which declined from 14% to 12.3%) and those pending approval (falling from 13.5% to 11%).

Reviewing the average distribution of the royalty across therapy area for those same transactions shows that deals including at least one hematology asset had the highest average royalty rates; at 26.1%, this represents a big increase from the former period's 5% [Figure 13]. During the last review period dermatology was the top category (after the others group) at a 14.5% average royalty, and although it fell to the middle of the chart this year, it still had an average 13.5% royalty rate.

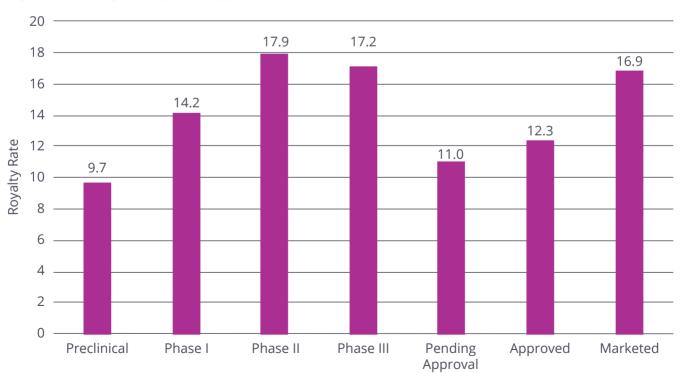


Figure 12. Average royalty rates by phase

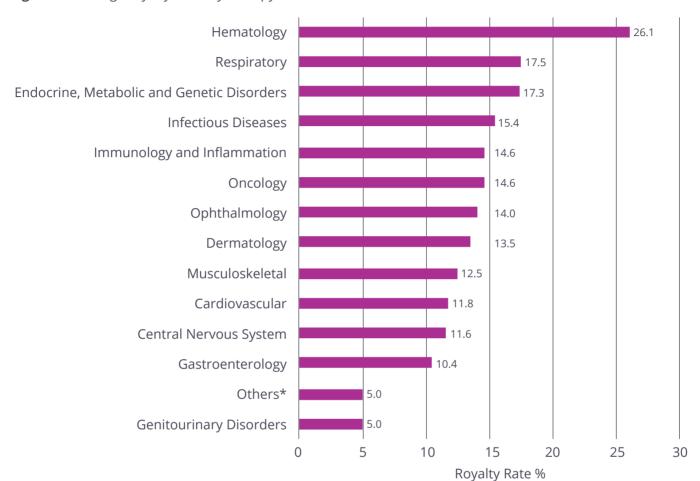


Figure 13 Average royalty rates by therapy area

*Others includes other therapy areas and selected medical device and diagnostics deals.

Source: Medtrack 2019

What's Next

Although deal volume remained steady from the last review period, the dollars skyrocketed and there appears to be no shortage of high-valued

partnerships. This year's BIO-Europe meeting is sure to result in the forging of many new partnerships, which we will continue to follow and analyze.



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