

Biotechnology Bring-on the Bounce Back; Top Ideas for 2017

Key Takeaway

We believe robust fundamentals should support further outperformance of EU biotech this year. A possible windfall of sector consolidation, exciting new technologies, and a favourable regulatory landscape are key potential drivers, plus we are optimistic concerns over draconian US pricing for biotech should somewhat abate, albeit political rhetoric remains a risk.

Stock ideas for 2017: Our top picks are Ablynx, AC Immune, Advanced Accelerator Applications, Genmab, NeuroDerm, and Shire. We also highlight potentially compelling risk-reward from upcoming binary events for Bavarian Nordic and Cassiopea. Our least preferred stock is UCB. For investors seeking a diversified approach to investing in the sector we highlight PureTech.

Notable changes: Downgrading Actelion to Hold (PT CHF240 +26%) given the challenge predicting if it will be acquired. Upgrading UCB to Hold (PT €65 +18%) as the current share price now fairly reflects our concerns on longevity of growth. Raising PTs on Buy rated Ipsen to €80, Lundbeck to DKK340, Galapagos to €80, Genmab to DKK1500, and Protalix to €1.20.

Potential sector drivers: (1) Sector consolidation particularly if the new US administration introduces cash repatriation. (2) Clinical data and potential launches of new technologies such as gene therapies, I-O combinations, and CAR-T. (3) Evolving and favourable regulatory landscape for drug approvals. (4) Concerns over draconian US drug pricing for biotech somewhat abate as innovation is still rewarded.

Brief 2016 re-cap: Our EU biotech composite rose +20% (+24% in Euro), significantly outpacing the broader DRG index and US peers, driven by big gains for the larger success stories such as Actelion and Genmab. Globally last year was tough for the sector, down 33% ex larger caps with 3/4 stocks declining.

In this report, we also outline key potential upcoming events for the EU biotech and biopharma sectors and have provided detailed updated catalyst calendars.

Company Name	Ticker	Mkt. Cap (MM)	Rating	Price [^]	Price Target	Cons. Next FY	Current EPS Estimates			Previous Est.	
							2015	2016	2017	2016	2017
Ablynx	ABLX BB	€668.7	BUY	€10.98	€21.00	--	€(1.00)	€(0.34)	€(0.68)	€(0.34)	€(0.68)
AC Immune	ACIU	\$756.2	BUY	\$13.65	\$25.00	--	CHF0.47	CHF(0.24)	CHF(0.63)	CHF(0.24)	CHF(0.63)
Actelion	ATLN VX	CHF23,433.3	HOLD ▼	CHF223.60	CHF240.00 ▲	--	CHF5.50	CHF7.61	CHF7.27	CHF7.59	CHF7.00
Adocia	ADOC FP	€387.6	BUY	€57.00	€100.00	--	€1.88	€(2.37)	€7.48	€2.85	€6.53
AAA	AAAP	\$1,199.0	BUY	\$27.25	\$45.00	--	\$(0.37)	\$(0.62)	\$(0.54)	\$(0.62)	\$(0.54)
ALK-Abello A/S	ALKB DC	DKK9,770.6	HOLD	DKK997.00	DKK900.00	--	DKK27.31	DKK30.45	DKK29.54	DKK31.39	DKK23.61
Almirall	ALM SM	€2,631.3	HOLD	€15.21	€16.00	--	€0.71	€0.84	€0.96	€0.82	€0.96
Bavarian Nordic	BAVA DC	DKK8,556.5	BUY	DKK272.50	DKK350.00	--	DKK3.72	DKK1.75	DKK40.52	DKK1.63	DKK37.75
BTG	BTG LN	£2,266.3	BUY	588.50p	860.00p	--	15.71p	21.85p	21.85p	21.85p	21.85p
Cassiopea	SKIN SW	CHF291.0	BUY	CHF29.10	CHF60.00	--	€(0.65)	€(1.99)	€(2.15)	€(1.99)	€(2.15)
Compugen	CGEN	\$266.2	BUY	\$5.10	\$9.00	--	\$(0.40)	\$(0.65)	\$(0.73)	\$(0.65)	\$(0.73)
Cosmo	COPN SW	CHF2,399.8	BUY	CHF170.20	CHF245.00	--	€(0.68)	€0.26	€0.12	€0.26	€0.12
Erytech	ERYP FP	€121.3	BUY	€14.97	€43.00	--	€(2.16)	€(2.71)	€(3.57)	€(2.71)	€(3.57)
Galapagos	GLPG NA	€2,905.8	BUY	€62.76	€80.00 ▲	--	(2.46)	(0.43)	(0.51)	(0.24)	(0.73)
Genmab	GEN DC	DKK74,654.4	BUY	DKK1,236.00	DKK1,500.00 ▲	--	DKK10.00	DKK15.80	DKK18.50	DKK14.80	DKK17.20
Ipsen	IPN FP	€5,922.7	BUY	€70.93	€80.00 ▲	--	€2.80	€3.11	€3.66	€3.10	€3.58
Lundbeck	LUN DC	DKK57,284.2	BUY	DKK289.90	DKK340.00 ▲	--	DKK0.66	DKK8.67	DKK14.28	DKK8.55	DKK13.13
Neuroderm	NDRM	\$608.5	BUY	\$23.05	\$42.00	--	\$(0.82)	\$(1.47)	\$(1.68)	\$(1.47)	\$(1.68)
Oxford BioMedica	OXB LN+	£128.2	BUY	4.15p	8.00p	--	(0.51)p	(0.53)p	(0.17)p	(0.53)p	(0.17)p
Poxel	POXEL FP	€169.2	BUY	€7.39	€12.00	--	€(0.69)	€(1.10)	€0.45	€(1.10)	€0.45
Protalix BioTherapeutics, Inc.	PLX	\$51.6	BUY	\$0.42	\$1.20 ▲	--	\$0.19	\$(0.36)	\$(0.21)	\$(0.36)	\$(0.30)
PureTech	PRTC LN+	£294.4	BUY	124.00p	255.00p	--	(13.92)p	(19.04)p	(23.12)p	(19.04)p	(23.12)p
Shire	SHP LN	£43,681.9	BUY	4,831.00p	6,600.00p	--	\$3.89	\$4.32	\$5.11	\$4.32	\$5.11
UCB	UCB BB	€12,512.2	HOLD ▲	€64.33	€65.00 ▲	--	€2.17	€3.08	€3.97	€3.08	€3.88
Zealand Pharma A/S	ZEAL DC	DKK2,949.3	BUY	DKK113.00	DKK190.00	--	DKK(4.94)	DKK(6.47)	DKK(8.81)	DKK(6.47)	DKK(8.81)

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[^] Prior trading day's closing price unless otherwise noted.

Best of Biotech into 2017

2016 was a turbulent year for the sector with the US NASDAQ Biotech index down -22% as around three quarters of stocks declined. In sharp contrast the European biotech sector significantly outperformed, largely driven by big gains for the success stories and bellwethers, notably Actelion and Genmab, assisted by relative FX tailwinds. We are optimistic robust fundamentals should ultimately support a better year of share price performance for the overall biotech sector in 2017. Potential drivers include: (1) Sector consolidation particularly if the new US administration introduces a repatriation plan for offshore cash; (2) Clinical data and potential launches of exciting new technologies and therapies such as gene therapies, immunoncology combinations, and chimeric antigen receptor T-cell (CAR-T); (3) Regulatory landscape remains favourable with both US FDA and European EMA willing to accept a degree of risk for new products notably for unmet medical needs; and (4) Concerns over draconian US drug pricing for biotech somewhat abate as innovation is still rewarded with premium reimbursement and payers continue to further implement their current strategies to curb inflating spend, such as tiering mechanisms and demanding discounts/rebates. We assume the capital markets remain selective but accessible for funding.

Table 1: Our 2017 stock ideas in Biotech and Biopharma

Top Biotech Picks	Possible Biotech	Top BioPharma	Least Preferred	Diversified
	Winners	Pick	Stock	Approach
Ablynx	Bavarian Nordic	Shire	UCB	PureTech
AC Immune	Cassiopea			
Advanced Accelerator Applications				
Genmab				
NeuroDerm				

Source: Jefferies research

Table 2: Notable changes to ratings and Price Targets

Stock		Rating		Price Target		
		New	Prior	New	Prior	
Actelion	Downgraded rating <i>Challenging to predict likelihood of company being successfully acquired</i>	Hold	Buy	CHF 240	CHF 190	+26%
UCB	Upgraded rating & PT <i>Share price now fairly reflects our concerns regarding the longevity of growth</i>	Hold	Underperform	€65	€55	+18%
Ipsen	Raised PT <i>Remain bullish on Somatuline sales trajectory for EPS +10-20% above consensus from 2018E</i>	Buy	Buy	€80	€65	+23%
Lundbeck	Raised PT <i>New product momentum should continue to drive share price appreciation</i>	Buy	Buy	DKK 340	DKK 260	+31%
Galapagos	Raised PT <i>Now assume \$3bn WW peak sales of CF triple combo, still at 20% probability, for higher Price Target</i>	Buy	Buy	€80	€67	+19%
Genmab	Raised PT <i>Updated FX rates raises Price Target</i>	Buy	Buy	DKK 1500	DKK 1400	+7%
Protalix	Raised PT <i>Confirmed orders of Uplyso in Brazil significantly boost our NPV and mitigate the cash shortfall risk</i>	Buy	Buy	\$1.20	\$0.80	+50%

Source: Jefferies research

This year we highlight six top picks within our coverage universe (Ablynx, AC Immune, Advanced Accelerator Applications, Genmab, NeuroDerm, and Shire), plus two biotechs with compelling risk-reward from upcoming binary events (Bavarian Nordic and Cassiopea). Our least preferred stock is UCB. For investors seeking a diversified approach to investing in the sector we highlight PureTech.

Top biotech picks – still attractive valuations and catalysts

- **Ablynx** (ABLYX BB, €10.7) – We still believe impressive Phase II TITAN caplacizumab results in rare blood disorder aTTP are a potential game-changer for Ablynx. Phase III results are expected by 4Q17E for a potential 1H19E US launch, with EU filing for conditional approval planned during 1Q17E for possible roll-out to begin from 1H18E. The ALX-0171 Phase IIIb dose-ranging efficacy study in infants hospitalised with RSV infection is expected to start during 1Q17E for data around 1H18E. Whilst AbbVie's (ABBV, \$62, Buy) decision not to opt-in to the RA indication for vobaniluzumab (anti-IL-6R) was disappointing, Ablynx is planning future development in parallel with seeking a new partner, a key potential catalyst for 2017E. Regulatory end-of-Phase II meetings are expected to take place during 1H17E, with the intention of starting a Phase III study by YE17E, subject to partnering. Finally, progress in other key collaborations with Merck (MRK, \$60, Underperform), Merck Serono (MRK GR, €101, NC), and Boehringer (private) could also provide catalysts for the shares, particularly the broad immuno-oncology deal with Merck that may drive significant upside.
- **AC Immune** (ACIU US, \$13) – AC Immune (ACIU) has perhaps the broadest Alzheimer's disease (AD) pipeline in biotech, in our view, with active and passive immunotherapies targeting both amyloid beta (Abeta) and tau, providing multiple multiblockbuster opportunities. Partner Genentech (part of Roche, ROG VX, CHF 263, Buy) has lead product crenezumab in Phase III for prodromal-mild AD with results during 2020E. Despite the recent Phase III failure of Lilly's (LLY, \$75, Buy) solanezumab, detailed data still lend support to the amyloid hypothesis, in our view, with key profile differences between the two anti-Abeta antibodies and trial designs potentially favouring crenezumab. Importantly, numerous pipeline catalysts could occur during 2017E, including: (1) Phase I/IIa data for fully-owned anti-Abeta vaccine ACI-24 during 1Q17E; (2) Phase Ib data for anti-Tau vaccine ACI-35 partnered with Janssen (part of JNJ, \$116, Hold); and (3) Phase I results for anti-Tau antibody RG6100 partnered Roche during 2Q17E. Positive results could see all three products enter Phase II development during 2H17E. Finally, the findings from an interim analysis of the API Columbia AD prevention study with crenezumab could potentially be disclosed around mid-2017E.
- **Advanced Accelerator Applications** (AAP US, \$27.2) – Targeted cancer therapy Lutathera is the key driver for the stock, in our view, promising to be a paradigm shift for treatment of advanced gastroenteropancreatic neuroendocrine tumours (GEP-NETs). Recent setbacks following the Complete Response Letter from the FDA and the prolonged EMA timeline were disappointing, however we still expect potential approvals around mid-2017E. We believe these regulatory delays reflect management's inexperience and importantly do not relate to concerns regarding Lutathera's impressive clinical benefit or safety profile. We are confident the product is already largely de-risked and has a significant commercial opportunity, transforming AAA as it launches the drug itself in US/EU. AAA's PET tracer companion diagnostic NETspot/Somakit for NETs has already been approved in the US and Europe. We also expect ongoing robust sales growth from the established portfolio of PET and SPECT tracers.

- **Genmab** (GEN DC, DKK 1204) – We are confident that Darzalex is already becoming entrenched in the multiple myeloma (MM) treatment paradigm, with recent positive Phase Ib PAVO subcutaneous data, unprecedented minimal residual disease (MRD) negativity data, and expedited FDA approvals for relapsed/refractory MM (RRMM) bolstering enthusiasm further during 2H16. 2017 should see no let-up to the Darzalex newsflow, with eagerly awaited results from the Phase II study in Non-Hodgkin’s Lymphoma potentially by mid-2017E, the Phase III ALCYONE interim analysis in first-line MM anticipated 3Q17E, and the Phase II study in smoldering MM by 4Q17E, all significant catalysts for the stock. Importantly, we should also see progress from Genmab’s pipeline, with two cancer antibodies expected to enter the clinic by YE17E, expanding the pipeline beyond HuMax-TF ADC, for which Phase I data are expected by mid-17E, and HuMax-AXL ADC also in Phase I.
- **NeuroDerm** (NDRM US, \$22.5) – The recently revised US development plans for NDO612L/H in Parkinson’s disease provides a lower risk and perhaps expedited pathway to approval, in our view. NDRM is now pursuing a comparative pharmacokinetic (PK) pathway in place of two Phase III efficacy studies, supported by long-term safety data from the ongoing BeyoND trial. NDRM is already pursuing this strategy in Europe. The European NDO612H PK ‘09 similarity trial versus Duodopa is expected to start during 1Q17E for data around 3Q17E, with US PK studies also expected to commence during early-2017E for data by YE17E. Long-term safety data from the BeyoND trial remain rate-limiting, anticipated 1H18E. Both NDO612L/H are liquid formulations of the current PD standard-of-care L-dopa/carbidopa. A convenient, continuous infusion of L-dopa could offer substantial clinical benefits for more advanced PD patients, avoiding the fluctuations of peak-dose dyskinesias and wearing-off, plus the potential for improved quality of sleep and delayed morning “on” given night-time dosing. This underscores our confidence for \$1.7bn WW peak sales and 2019E launches, suggesting significant upside from the current share price.

Possible biotech winners – significant upside from upcoming binary events

- **Bavarian Nordic** (BAVA DC, DKK 269) – Prostate cancer immunotherapy PROSTVAC remains the long-term value driver with the third and final Phase III interim survival (OS) analysis expected around mid-2017E and final data by YE17E. The likelihood of safety concerns is now remote, in our view, as all subjects are receiving standard-of-care. Hence we believe the most likely scenarios are either that the trial continues beyond the third interim until the final readout, or “best” case determines PROSTVAC has demonstrated a significant benefit, suggesting asymmetric upside during the next six months. The BMS (BMY, \$59, Hold) deal provided some third-party validation on the wealth of Phase I-II data, Phase III plan, and technology platform, as well as facilitating the expedited initiation of further clinical trials in combination with checkpoint inhibitors. Other catalysts that could drive outperformance are: (1) Data from the Phase II trial of MVA-BN RSV vaccine in elderly during 2H17E, for initiation of a Phase IIb field trial by YE17E; (2) Additional MVA-BN Ebola vaccine clinical data, with initial results from the Phase III EBOVAC-Salone field trial and partner Janssen opting-in to develop other vaccines; (3) Initiation of further trials of CV-301 in combination with immuno-oncology drugs; and, (4) incremental government contracts for MVA-BN Ebola and IMVAMUNE smallpox vaccine stockpiles. We believe a number of these potentially important catalysts for the shares are widely overlooked.

- **Cassiopea** (SKIN SW, CHF 29.4) – Given the multi-billion dollar US acne market, we believe lead product Winlevi has substantial commercial potential for Cassiopea, providing the foundation for a highly profitable US dermatology franchise. Phase III data in moderate to severe acne are expected in 3Q17E, for potential filing by YE17E, providing a significant catalyst for the stock this year which could significantly boost our valuation. If positive, Winlevi could be the only topical anti-androgen therapy approved, avoiding the systemic side-effect issues that limit use of oral alternatives. Our physician channel checks suggest possible rapid and widespread adoption, mostly as an integral part of the combination regimens typically prescribed to treat this multi-faceted disease. Other pipeline catalysts include the start of a Phase IIIb trial of Breezula for alopecia in early 2017E and the Phase IIIb trial of CB-06-01 for acne during 1H17E, along with CB-06-02 Phase II data for anogenital warts during 3Q17E.

Top biopharma pick

- **Shire** (SHP LN, 4760p) – Robust +14% long-term EPS growth, at a minimum, aided by the successful integration of Baxalta, plus future upside from the late-stage pipeline, underpins our positive outlook for the stock. We remain confident in the sustainability of the Haemophilia franchise, and believe widespread fears on pricing and competition are likely overdone. Significant Phase II-III pipeline news during 2017 could heighten confidence in Shire's long-term organic growth prospects, including: (1) SHP643 Phase III data in hereditary angioedema (HAE) around mid-2017E for potential filings by YE17E; (2) Re-filing and potential US approval of SHP465 for adult ADHD around mid-2017E; (3) Start of Phase III trial of SHP640 for acute conjunctivitis in early-2017E; and, (4) Start of the Phase III trial of SHP607 in preterm infants by YE17E. These, along with other pipeline catalysts, together with a high likelihood of synergistic business development deals, further boost belief in double-digit earnings CAGR until at least 2020E. Given the scarcity value for high-quality growth companies in the sector, particularly with some long duration assets, we believe the current share price significantly undervalues Shire.

Least preferred stocks

- **UCB** (UCB BB, €62) – Phase III ARCH data for romosozumab (anti-sclerostin antibody) in post-menopausal osteoporosis (PMO) are expected during 2Q17E, with a focus on the drug's benefit reducing non-vertebral fractures as the FRAME trial missed this potentially commercially important endpoint. We anticipate US approval around the 19 July FDA PDUFA date. The marked effect demonstrated by romosozumab in the FRAME trial after only 12 months treatment suggests an important future role for the drug in the PMO treatment paradigm, in our view. However, we believe the current share price already reflects romosozumab success for blockbuster sales, as well as ongoing growth of core CVN (Cimzia, Vimpat and Neupro) products, and targeted REBITDA margin expansion to 30% by 2018E. Hence, we believe focus is shifting beyond the current period to assessing the longevity of growth. We remain enthusiastic on steady growth of epilepsy drug Vimpat, assuming no generic erosion until the 2022E patent expiry after the District Court ruling in favour of UCB in August 2016. We retain a more cautious stance on Cimzia in view of longer-term risks from competing oral drugs and anti-TNF α biosimilars, which could increasingly gain traction as a focus for investors during 2017E. We believe the current share price now reflects these concerns, hence we are upgrading to Hold with a €65 per share price target (+18%).

Attractive diversified approach to investing in the sector

- **PureTech** (PRTC LN, 124p) – PureTech aims to apply novel concepts to address unmet medical needs, sourcing ideas from its network of world-leading scientific advisors to form new portfolio companies. Over the next 12-18 months, we foresee a number of key catalysts for the portfolio that could ultimately crystallise value. Three Growth Stage Operating Companies in the portfolio that we highlight are: (1) Vedanta aiming to modulate the human microbiome, with widespread enthusiasm for drugs harnessing this approach still largely underappreciated by the current valuation, in our view; (2) Akili seeking to measure and improve cognition and executive function across patient populations using a novel and cost-effective technology based on a video game; and (3) Gelesis developing a product that acts mechanically in the gastrointestinal tract to be a safe and effective treatment for obesity.

Key upcoming events

For investors seeking near-term catalysts we highlight the following in our biotech and biopharma sectors, for which we are on balance positive on the majority.

Table 3: Key potential upcoming catalysts for biotech and biopharma stocks under coverage

Ablynx	Caplacizumab Phase III aTTP data by YE17E Our view = +: Encouraged by impressive Phase II data providing important clinical benefit
AC Immune	Phase I data for ACI-24, ACI-35 and RG6100 to enable start of Phase II programmes Our view = +: Preclinical data and initial results suggest safe and well-tolerated
Adocia	Partner Eli Lilly advancing BC Lispro into Phase III trials Our view = +: Initial Phase Ib-IIa trials have all been positive and Eli Lilly seems committed
AAA	Lutathera EU and US approvals for GEP-NETS Our view = +: Impressive Phase III data suggest high likelihood of approvals around mid-2017E
ALK Abello	US approval of house dust mite SLIT-tablet in 1Q17E Our view = +: Positive Phase III data and already marketed in Europe suggesting approval likely
Bavarian Nordic	PROSTVAC Phase III PROSPECT trial third interim analysis by mid-2017E and final data in mCRPC by YE17E Our view = +/-binary: Optimistic for efficacy but evolving treatment paradigm means difficult to call
Cassiopea	Winlevi Phase III results in acne during 2H17E Our view = +: Novel mechanism of action and impressive Phase II data bolsters confidence
Cosmo	Remimazolam Phase III bronchoscopy data during 1H17E Our view = +: Prior successful completion of Phase III in colonoscopy suggests success likely
Erytech	GRASPA Phase II data in pancreatic cancer during 1Q17E Our view = binary: High risk indication which is notoriously difficult to treat GRASPA Phase IIb data in first-line AML by YE17E Our view = binary: Passed 3 interim safety analyses; small trial size means demonstrating significance difficult
Galapagos	Progressing CF triple combination therapy into patients by mid-2017E Our view = binary: Confident in predictive platform, but ambitious timeline dependent upon multiple readouts
Genmab	Darzalex Phase II data in NHL in mid-2017E Our view = +: Data suggest recruits immune system suggesting potential for use in multiple cancer indications Darzalex ALCYONE Phase III potential interim analyses in first-line MM (3Q17E) and Phase II SMM data (4Q17E) Our view = +: High likelihood of success given impressive clinical data in other MM settings to-date
Ipsen	Dysport new indications and Next Generation pre-filled syringe regulatory progress during 2017E Our view = +: Anticipate EU approvals in ALL & PLL and US approval in ALL plus filings of NG in EU & Brazil
Lundbeck	Rexulti Phase III agitation-dementia data during 2H17E Our view = +/-binary: Cautiously optimistic given clinical data to-date and promising tolerability profile
Neuroderm	ND0612L/H bioequivalence results vs. Duodopa in EU and US during 2017E Our view = +: High likelihood of success given earlier positive PK bioequivalence data
Oxford BioMedica	Novartis US filing of CTL019 for paediatric ALL in early-2017E, for potential FDA approval by YE17E Our view = +/-binary: Optimistic given promising data but novel therapy may raise regulatory concerns
Poxel	Imeglimin Phase IIb Japan T2D results Our view = +: High likelihood of success given earlier positive Phase II trials
Shire	SHP465 US re-filing for adult ADHD in early-2017E for potential approval in 3Q17E Our view = +: Positive paediatric Phase III data should satisfy FDA and reinforce our confidence in approvability SHP643 Phase III data in HAE Our view = +: Optimistic on potential to improve efficacy and convenience vs SOC; no safety signals to date
UCB	Romosozumab Phase III osteoporosis ARCH data and potential US approval for PMO around mid-2017E Our view = +: Data to-date demonstrate marked effect after only 12 months, suggesting approval likely

Source: Jefferies estimates

Table 4: EU biotech in 2016

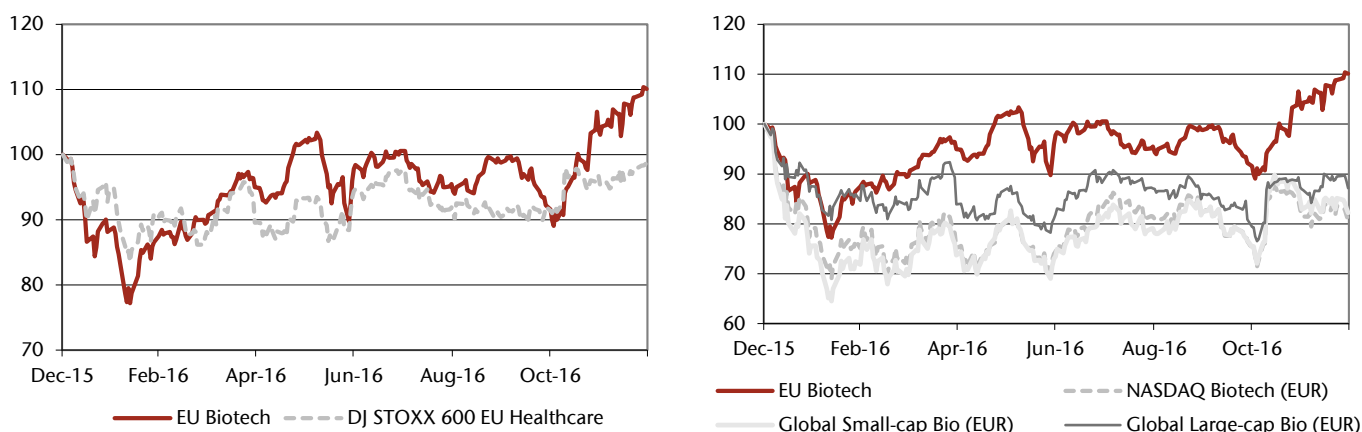
YTD 2016	% stocks
>+50%	9%
+20-50%	5%
+0-20%	18%
-0-20%	18%
-20-50%	36%
<-50%	14%

Source: Jefferies & FactSet

EU bellwethers outperformed in 2016

Last year our European biotech sector composite was up +20% (+24% in Euro), outperforming the broader healthcare sector DRG, mostly in 4Q (left side of Chart 1). For the second year in a row the group again outperformed the US sector (right side of Chart 1), with Global Large-caps down 12% and the Small-cap subsector falling by a third in USD. We note the European sector's gain was driven by big gains for the success stories and impressive performance by the larger stocks, as only a third of companies ended the year up. Approximately 9% of European biotechs rose over +50% in 2016.

Chart 1: European biotech significantly outperformed the Healthcare DRG and the US sector



Source: Jefferies and FactSet. Data updated 4 January 2017

Table 5: The ten best and worst EU biotech stocks by 2016 stock performance

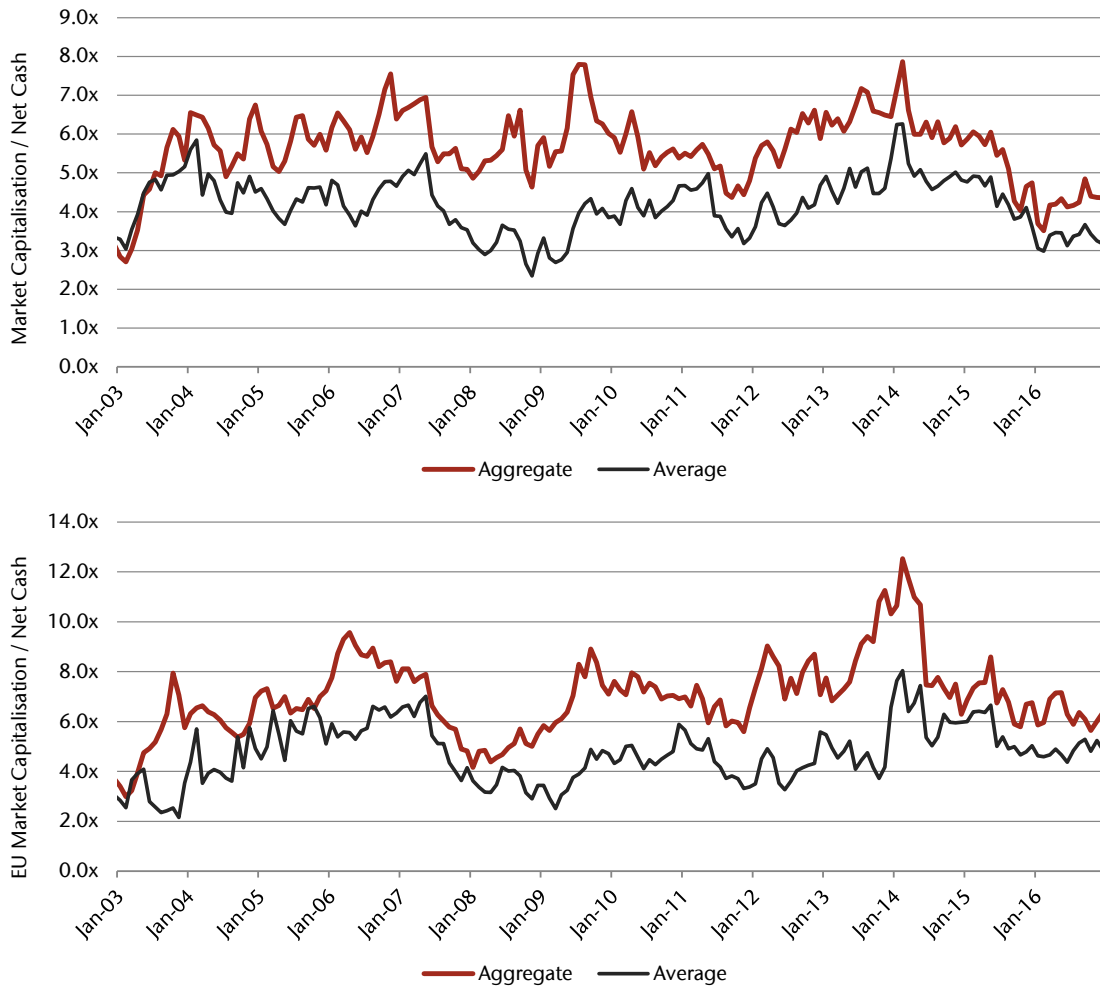
Top 10 performers		Worst 10 performers	
	2016 % change		2016 % change
Nordic Nanovector ASA	+586%	e-Therapeutics plc	-72%
PCI Biotech Holding ASA	+401%	Circassia Pharmaceuticals Plc	-71%
Sareum Holdings plc	+305%	MOLOGEN AG	-67%
Immunovia AB	+171%	Biophytis SA	-66%
Epigenomics AG	+105%	Proteome Sciences plc	-65%
GW Pharmaceuticals PLC	+85%	TxCell SA	-64%
Evotec AG	+78%	Novacyt SAS	-63%
ImmuPharma plc	+73%	Celyad SA	-63%
Biofrontera AG	+73%	Gentecel SA	-62%
Actelion Ltd.	+58%	XTL Biopharmaceuticals Ltd.	-61%

Source: Jefferies and FactSet as of 4 January 2017

It is difficult to quantify valuations for the small-cap biotech sector, particularly relative to historical levels. We believe a simple but instructive metric is the sector's Market Capitalisation to Net Cash; i.e. the Pipeline Value implied by the current share price.

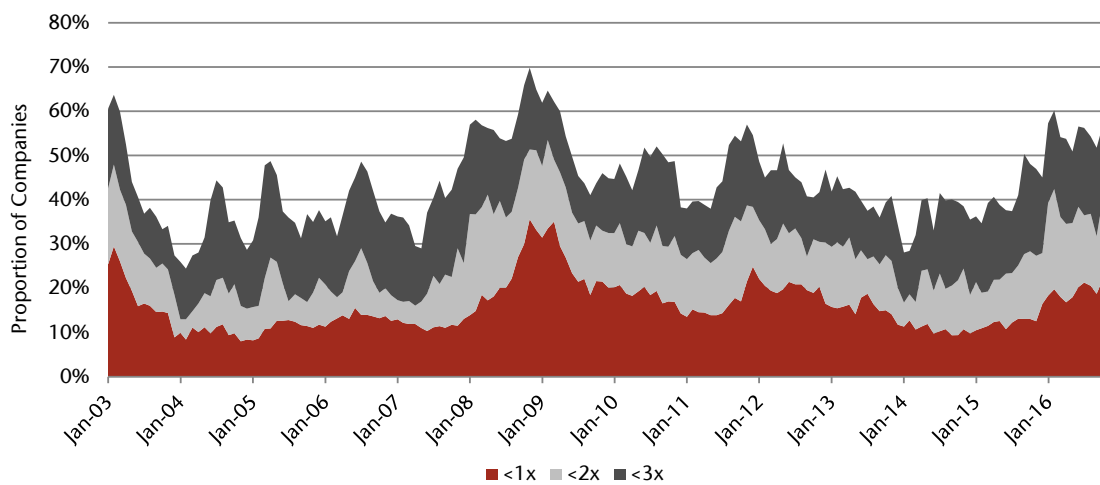
We are optimistic about the R&D output of biotech and our analysis suggests that on this metric both the Global Small-cap and European Biotech sectors are trading just below their average multiples (Chart 2). Globally around 25% of biotechs are trading below Net Cash, a proportion that has risen during the year well above the historic c.10% floor level (Chart 3).

Chart 2: Relative to Net Cash the Global (top) and EU (bottom) biotech sectors are trading just below their averages



Source: Jefferies and FactSet. Data updated 3 January 2017

Chart 3: The proportion of biotechs globally trading below 1x cash is c.25%, above the typical floor level of c.10%



Source: Jefferies and FactSet. Data updated 3 January 2017

Our EU Biotech Coverage Universe

We base our stock recommendations on a number of considerations including:

- **Valuation:** Based on probability-adjusted net present values (NPVs) for marketed and late-stage products, together with adjusted net cash. We do not normally include products in our sum-of-the-parts valuation prior to the availability of proof-of-concept data.
- **Upside/Downside to NPVs over the next 12 months:** We flex our NPVs based on key news flow events anticipated over a 12-month period; including clinical trial data, out-licensing deals, sales profiles on launch, competitor products and regulatory decisions. We believe catalysts that can drive upside to a valuation are essential for a stock to outperform, whereas in periods absent of news, shares will tend to be range-bound at best.
- **Funding requirements:** We assess the risk of a company needing to raise additional funds to prevent a cash shortfall. Market risk aversion and the equity funding window are likely to determine the discount applied to fundamental valuations for biotechs with potential future cash calls, in our view.

Table 6: Biotech stock coverage universe

Company	Price	Price Currency	Mkt Cap (\$m)	Mkt Cap (m)	Rating	Price Target	Upside/ (Downside)	Performance		
								1 Week	1 Month	1 Year
Ablynx	10.7	EUR	677	652	Buy	21	96%	1%	9%	-33%
AC Immune	13.0	USD	721	721	Buy	25	92%	-4%	13%	n/a
Adocia	59.8	EUR	425	409	Buy	100	67%	9%	20%	-18%
Advanced Accelerator Applications	27.2	USD	1,190	1,190	Buy	45	66%	3%	-8%	-13%
Bavarian Nordic	269.0	DKK	1,178	8,434	Buy	350	30%	14%	19%	-25%
BTG	596	GBP	2,807	2,293	Buy	860	44%	3%	4%	-14%
Cassiopea	29.4	CHF	286	294	Buy	60	104%	2%	2%	-10%
Compugen	5.1	USD	260	260	Buy	9	76%	-5%	-14%	-20%
Cosmo	169.5	CHF	2,328	2,396	Buy	245	45%	0%	-2%	5%
Erytech	14.3	EUR	118	114	Buy	43	200%	12%	16%	-44%
Galapagos	62.4	EUR	2,996	2,885	Buy	80	28%	2%	13%	10%
Genmab	1,204	DKK	10,150	72,661	Buy	1500	25%	3%	2%	31%
Neuroderm	22.5	USD	592	592	Buy	42	87%	1%	45%	32%
Oxford BioMedica	4.2	GBP	158	129	Buy	8	92%	4%	20%	-36%
Poxel	7.2	EUR	172	166	Buy	12	66%	4%	11%	-45%
Protalix	0.42	USD	51	51	Buy	1.20	189%	18%	34%	-59%
Zealand Pharma	109.0	DKK	398	2,850	Buy	190	74%	2%	-2%	-28%

Company	Market Cap /NPV	Net Cash as % Market Cap			EV/Sales				P/E			
		2016	2017	2018	2016	2017	2018	2019	2016	2017	2018	2019
Ablynx	50%	22%	14%	7%	5.8	10.0	7.9	5.5	n/a	n/a	n/a	n/a
AC Immune	54%	20%	16%	8%	25.3	28.7	95.3	n/a	n/a	n/a	n/a	n/a
Adocia	59%	12%	22%	28%	14.8	3.4	4.5	1.3	n/a	8.0	20.0	5.0
Advanced Accelerator Applications	61%	19%	17%	19%	8.5	6.2	3.7	2.1	n/a	n/a	79.4	22.9
Bavarian Nordic	73%	23%	34%	41%	6.0	1.8	2.5	2.7	153.5	6.6	15.9	26.1
BTG	69%	6%	7%	12%	4.8	3.8	3.1	2.6	27.3	27.2	15.9	12.9
Cassiopea	48%	10%	2%	-7%	n/a	n/a	9.7	9.3	n/a	n/a	n/a	n/a
Compugen	49%	22%	9%	3%	243.4	36.0	31.6	1,485.0	n/a	n/a	n/a	n/a
Cosmo	70%	4%	3%	2%	33.7	21.5	14.3	8.0	603.2	1,365.4	800.6	35.8
Erytech	24%	23%	1%	-35%	22.5	39.6	14.2	20.3	n/a	n/a	n/a	n/a
Galapagos	77%	33%	29%	26%	12.4	11.1	9.9	6.9	n/a	n/a	170.9	28.9
Genmab	81%	5%	8%	11%	39.2	32.3	19.6	11.8	76.2	65.1	33.1	23.3
Neuroderm	53%	26%	19%	16%	n/a	n/a	10.0	33.8	n/a	n/a	n/a	n/a
Oxford BioMedica	51%	-8%	-12%	-14%	5.2	4.5	4.2	3.6	n/a	n/a	n/a	n/a
Poxel	51%	27%	29%	14%	n/a	2.6	n/a	n/a	n/a	16.1	n/a	n/a
Protalix	24%	-53%	-96%	-126%	9.8	3.8	3.9	1.0	n/a	n/a	n/a	1.6
Zealand Pharma	57%	10%	3%	-3%	11.1	9.9	8.4	3.3	n/a	n/a	n/a	15.8
<i>Average</i>	<i>56%</i>	<i>12%</i>	<i>6%</i>	<i>0%</i>	<i>31.6</i>	<i>14.3</i>	<i>15.2</i>	<i>106.5</i>	<i>215.1</i>	<i>248.1</i>	<i>162.3</i>	<i>19.1</i>
<i>Median</i>	<i>54%</i>	<i>19%</i>	<i>9%</i>	<i>8%</i>	<i>11.7</i>	<i>9.9</i>	<i>9.0</i>	<i>5.5</i>	<i>114.9</i>	<i>21.7</i>	<i>33.1</i>	<i>22.9</i>

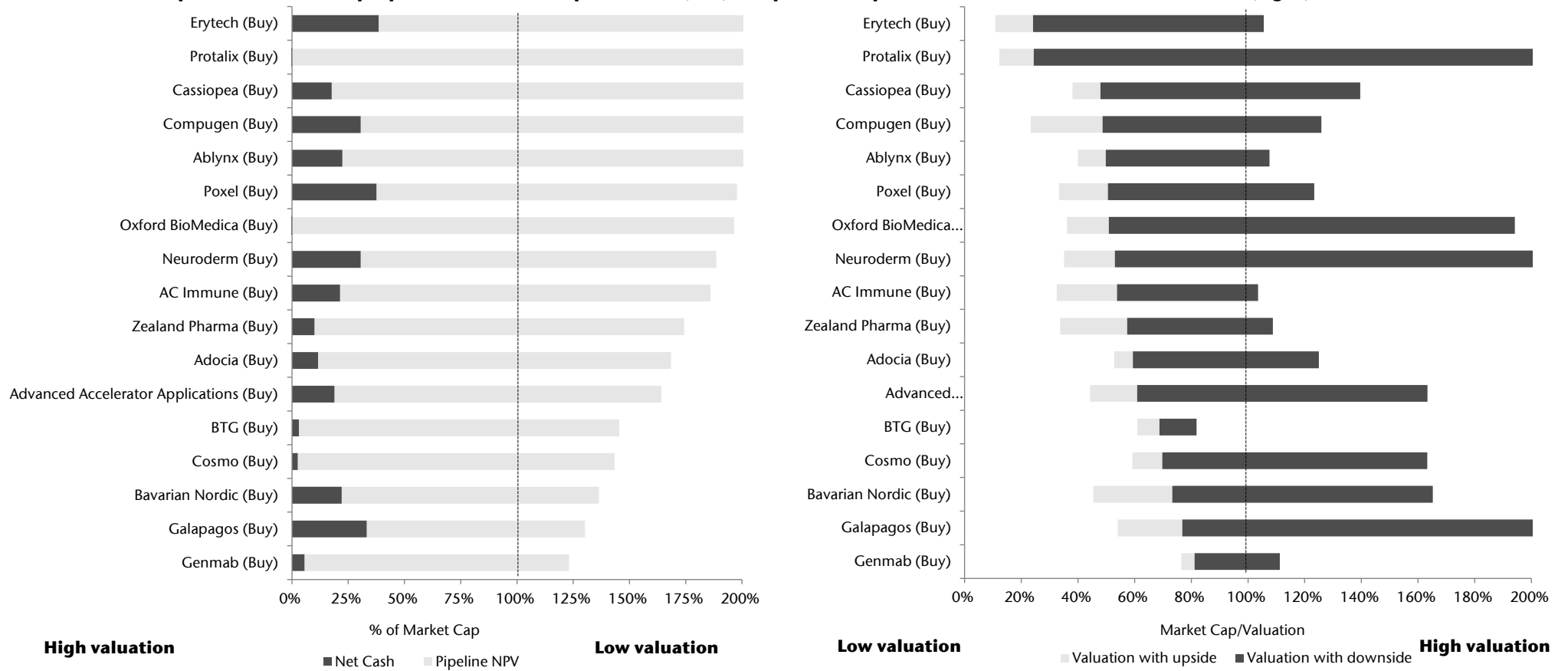
Source: Jefferies and FactSet. Stock prices as of close on 3 January 2017. All values are estimates

Healthcare

Rating | Target | Estimate Change

5 January 2017

Chart 4: Sum-of-the-parts valuation as a proportion of market capitalisation (left) and potential upside and downside risk to our valuations (right)



Source: Jefferies estimates

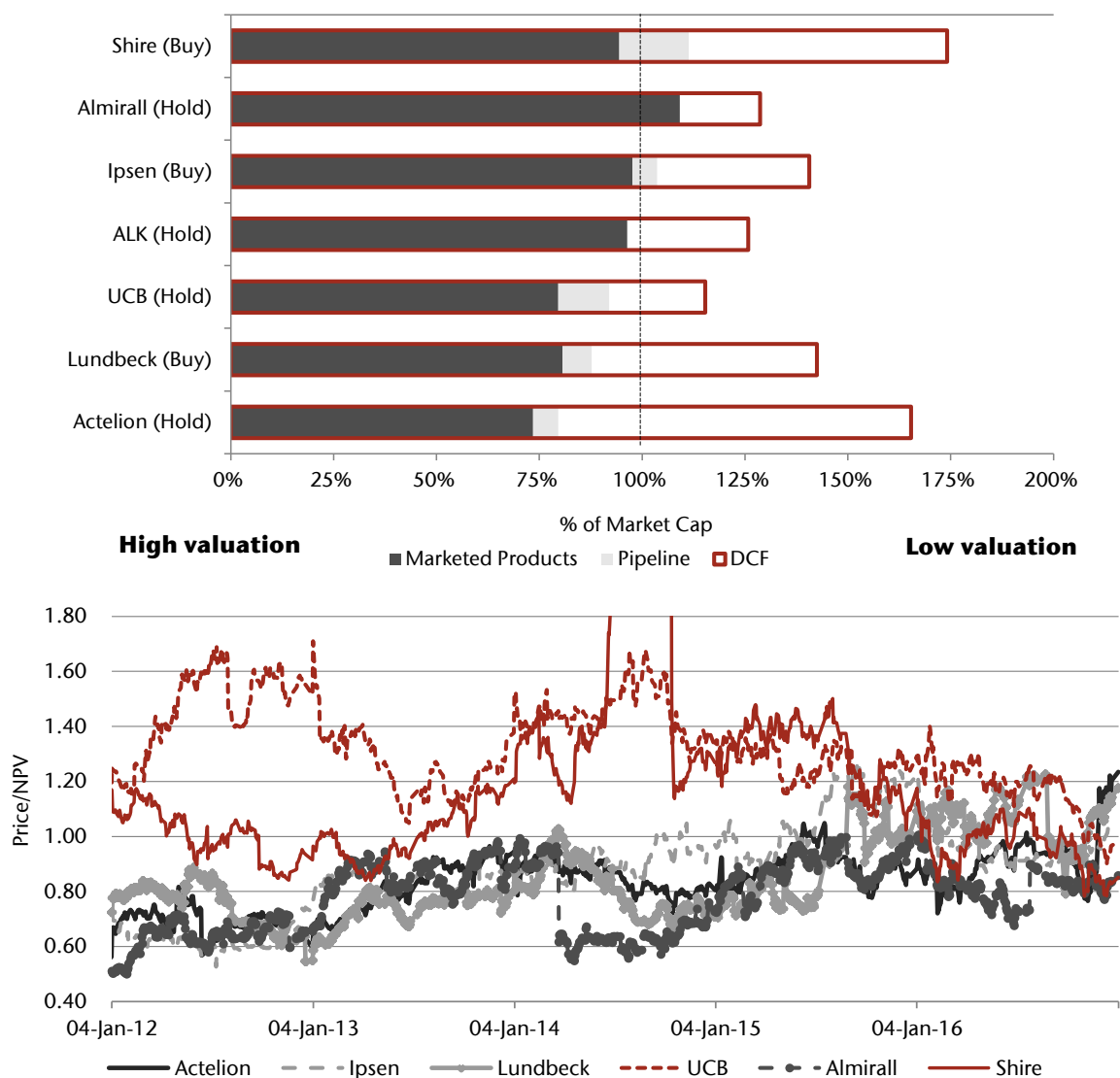
Our EU Biopharma Coverage Universe

Table 7: European Biopharma comps

Company	FactSet		Rating	Price		PE				CAGR 2016-19E		3 Yr PEG
	Ticker	Mkt Cap (\$m)		Currency	Price	2016E	2017E	2018E	2019E	EPS	Sales	2016
Actelion	ATLN-CH	23,533	Hold	CHF	224.7	30.4	31.9	24.7	19.0	17%	10%	1.8
Ipsen	IPN-FR	5,975	Buy	EUR	68.9	22.2	18.9	15.5	12.9	20%	11%	1.1
Lundbeck	LUN-DK	8,121	Buy	DKK	294.2	34.0	20.6	16.1	15.4	30%	5%	1.1
Shire	SHP-GB	52,685	Buy	GBP	4,760	13.9	11.4	9.8	8.5	18%	17%	0.8
UCB	UCB-BE	12,524	Hold	EUR	62.0	20.1	15.6	12.9	11.3	21%	6%	0.9
EU Biopharma Mid Cap						24.1	19.7	15.8	13.4	21%	10%	1.2
ALK	ALK.B-DK	1,223	Hold	DKK	951	31.2	32.2	31.3	29.5	2%	4%	

Source: Jefferies and FactSet. Stock prices as of close on 3 January 2017. All values are estimates

Chart 5: Price/NPV for our European Biopharma universe



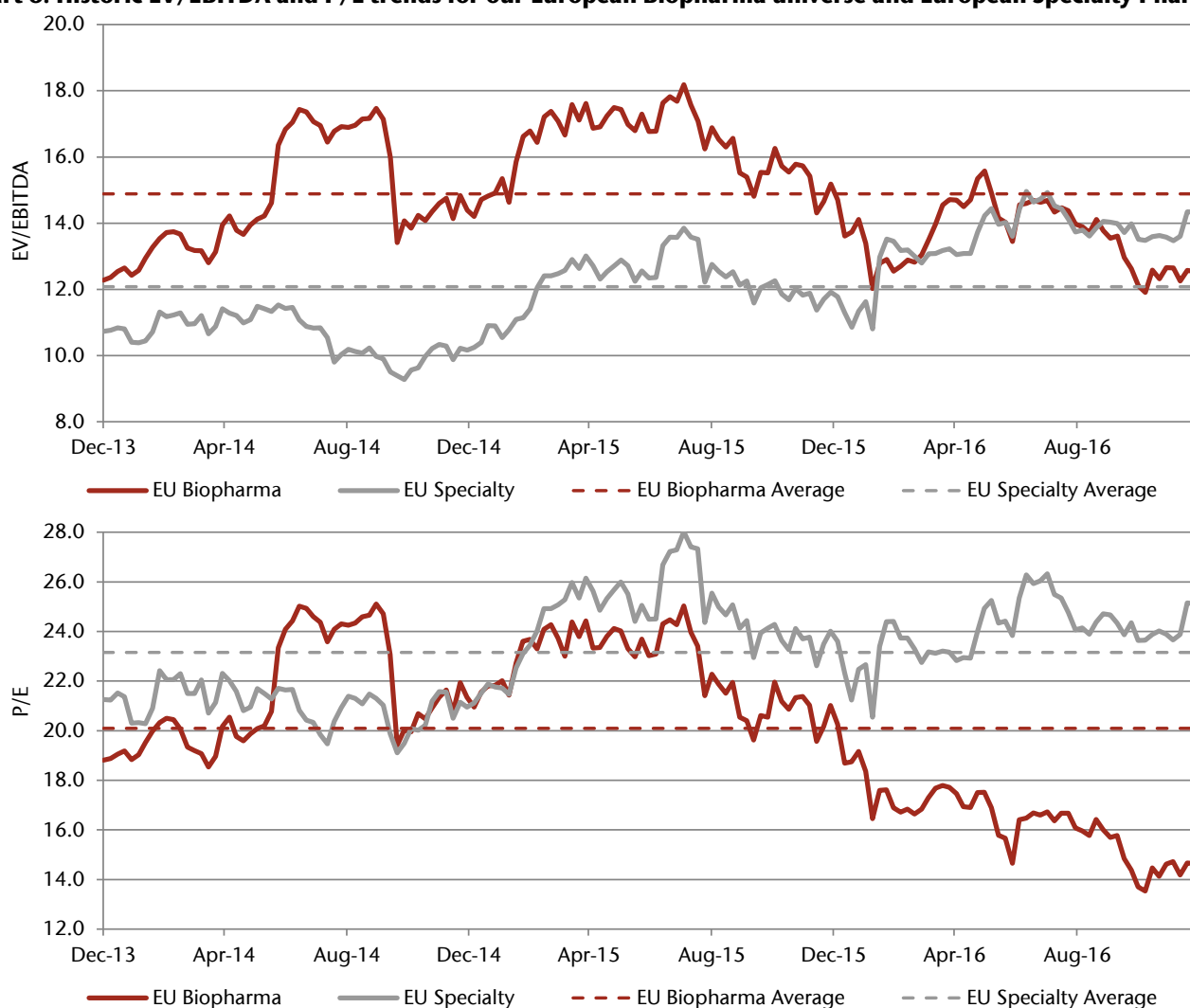
Source: Jefferies and FactSet. Stock prices as of close on 3 January 2017. All values are estimates

Table 8: PEG valuations for our European Biopharma universe and implied upside/downside to current share prices

Company	FactSet		Rating	Price		PEG Valuation			Upside/Downside
	Ticker	Mkt Cap (m)		Currency	Price	Year	Ratio	Value	
Actelion	ATLN-CH	23,542	Hold	CHF	224.7	2018	1.2	220.0	-2%
ALK	ALK.B-DK	9,350	Hold	DKK	951	2018	2.0	911	-4%
Almirall	ALM-ES	2,618	Hold	EUR	15.1	2018	1.6	13.7	-10%
Ipsen	IPN-FR	5,754	Buy	EUR	68.9	2018	1.2	80.3	+17%
Lundbeck	LUN-DK	58,140	Buy	DKK	294.2	2018	1.2	337.8	+15%
Shire	SHP-GB	43,040	Buy	GBP	4,760	2018	1.2	6,518	+37%
UCB	UCB-BE	12,061	Hold	EUR	62.0	2018	1.2	65.5	+6%

Source: Jefferies and FactSet. Stock prices as of close on 3 January 2017. All values are estimates

Chart 6: Historic EV/EBITDA and P/E trends for our European Biopharma universe and European Specialty Pharma



Source: Jefferies and FactSet. Stock prices as of close on 3 January 2017. All values are estimates

Changes to Ratings and Price Targets

UCB – Upgrade to Hold (from Underperform), PT +11% to €65

We believe the current share price now reflects our concerns regarding the longevity of growth, notably for Cimzia in view of longer-term risks from competing oral drugs and anti-TNF α biosimilars, hence we are upgrading to Hold. In-line with other stocks in our Biopharma coverage universe we now assume a 2018E 1.2x PEG to derive a Price Target of €65 per share, +18% from the prior €55.

Actelion – Downgrade to Hold (from Buy), PT +26% to CHF 240

Actelion's share price has risen c.40% since speculation first surfaced late November in the media that it was subject to a takeover bid and the company stated on 21 December that it had entered into exclusive negotiations with JNJ regarding a possible strategic transaction. It is challenging to predict the likelihood Actelion is acquired, in our view, hence given the share price rally we are downgrading to Hold. Our revised Price Target of CHF 240 per share reflects an equal blend of a fundamental CHF 220 per share assuming a 1.2x 2018E PEG ratio and the CHF 260 acquisition price reported in the press.

Lundbeck – PT raised +31% to DKK 340

Similar to other stocks in our Biopharma coverage universe, we now assume a 1.2x 2018E PEG ratio to derive a DKK 340 per share Price Target, +31% from the prior DKK 260 per share. We forecast an impressive earnings CAGR sustainable beyond 2020E, even with a heavily risk-adjusted pipeline. We expect new product momentum to drive continued share price appreciation, hence our Buy rating.

Ipsen – PT raised +23% to €80

Similar to other stocks in our Biopharma coverage universe, we now assume a 1.2x 2018E PEG ratio to derive a €80 per share Price Target, +23% from the prior €65 per share. Our Product Sales are around +6-12% above consensus from 2018E, mostly on a more bullish Somatuline trajectory for blockbuster peak sales based on our deep dive into the NET market, for +10-20% higher EPS. Ipsen's profitability falls below EU biopharma peers, mainly due to high S&M spend, but we believe its US subsidiary should drive an inflection from the current depressed levels.

Genmab – updating estimates for milestone payment; PT +7% to DKK 1500

In December Genmab announced that partner Janssen had submitted a regulatory application in Japan for daratumumab to treat RRMM, triggering a \$10m milestone payment. We have updated our model for this Revenue and current FX rates. Our Price Target rises a modest +7% to DKK 1500 from DKK 1400 per share.

Galapagos – updated peak sales of triple combo in CF; PT +19% to €80

We are raising our Price Target +19% to €80 from €67 per share as we now assume \$3bn WW peak sales of the triple combination in cystic fibrosis, raised from the prior overly conservative \$1bn placeholder. We retain a 20% probability of success, for a €13/share NPV contribution from €5/share.

ALK – model updated to reflect ongoing EU momentum; PT unchanged

ALK continues to benefit from market share gains in Southern Europe on supply constraints following the forced suspension of manufacturing and a product recall by key competitor Stallergenes Greer (STAGR FP, €31, NC) in early December 2015. ALK was quick to capitalise on its competitor's misfortune, and although STAGR has since resumed production and distribution the tailwind continues. 3Q Revenues were better than we had anticipated and management recently noted 4Q sales were above expectations, triggering another upgrade to the full year outlook. We have updated our model to reflect the ongoing positive momentum in the European base business.

Ablynx – voba probability in RA reduced to 40% from 50%; PT unchanged

Following AbbVie's decision not to opt-in to vobarilizumab for the RA indication, we have reduced our probability of success to 40% from 50%. Whilst Ablynx is planning for future development, a Phase III trial will require successfully partnering the product. Our €21 per share Price Target is unchanged.

Adocia – delaying BC Lispro milestone income into 2017E; PT unchanged

We had anticipated partner Eli Lilly to initiate a Phase III programme for BC Lispro by YE16E but now expect this could occur during 2017E.

Bavarian Nordic – higher YE16E cash balance; PT unchanged

We have updated our model for FX rates and to include the earlier cash receipt from the US Government for shipments of IMVAMUNE smallpox vaccine. Accordingly, our YE16E cash balance is increased. Our DKK 350 per share Price Target is unchanged.

Protalix – updating estimates to reflect Brazil order, PT +50% to \$1.20

In December, Protalix announced that the Brazilian Ministry of Health has confirmed an order for Uplyso (alfataliglycerase) totalling c.\$24.3m for 2017. The order consists of a number of shipments, starting in mid-2017 and continuing throughout the year in increasing volumes. To-date orders from the Brazilian Ministry have been small, thus this order far exceeds our prior 2017E estimate of \$7m. We have updated our model for 2017E and beyond accordingly, and as a result increase our PT +50% to \$1.20 per share.

We also note that on 3 January Protalix announced positive interim results from the Phase II clinical trial of PRX-110 (alidornase alda or AIR DNase) for the treatment of cystic fibrosis (CF). The 28-day switch-over study is evaluating the safety and efficacy of PRX-110 in CF patients previously treated with Pulmozyme, with a two-week washout period from Pulmozyme followed by treatment with PRX-110 via inhalation. Data from the first 13 CF patients, of 15 total, demonstrate that PRX-110 improved lung function as demonstrated by a mean absolute increase in the percent predicted forced expiratory volume in one second (ppFEV1) of 4.1 points from baseline. Sputa analysis from around 50% of patients demonstrate a c.60% mean reduction in DNA content from baseline, and a c.90% mean reduction in sputa visco-elasticity from baseline. Importantly, no serious adverse events were reported, and all adverse events that occurred during the study were mild and transient in nature. Full results from the study are expected by end-1Q17E.

Notable recent US list price rises

A number of companies in our coverage universe have recently increased US list prices on key products. We note that discounts and rebates may mitigate the true effect of these price rises.

Table 9: Notable US list price rises in recent weeks

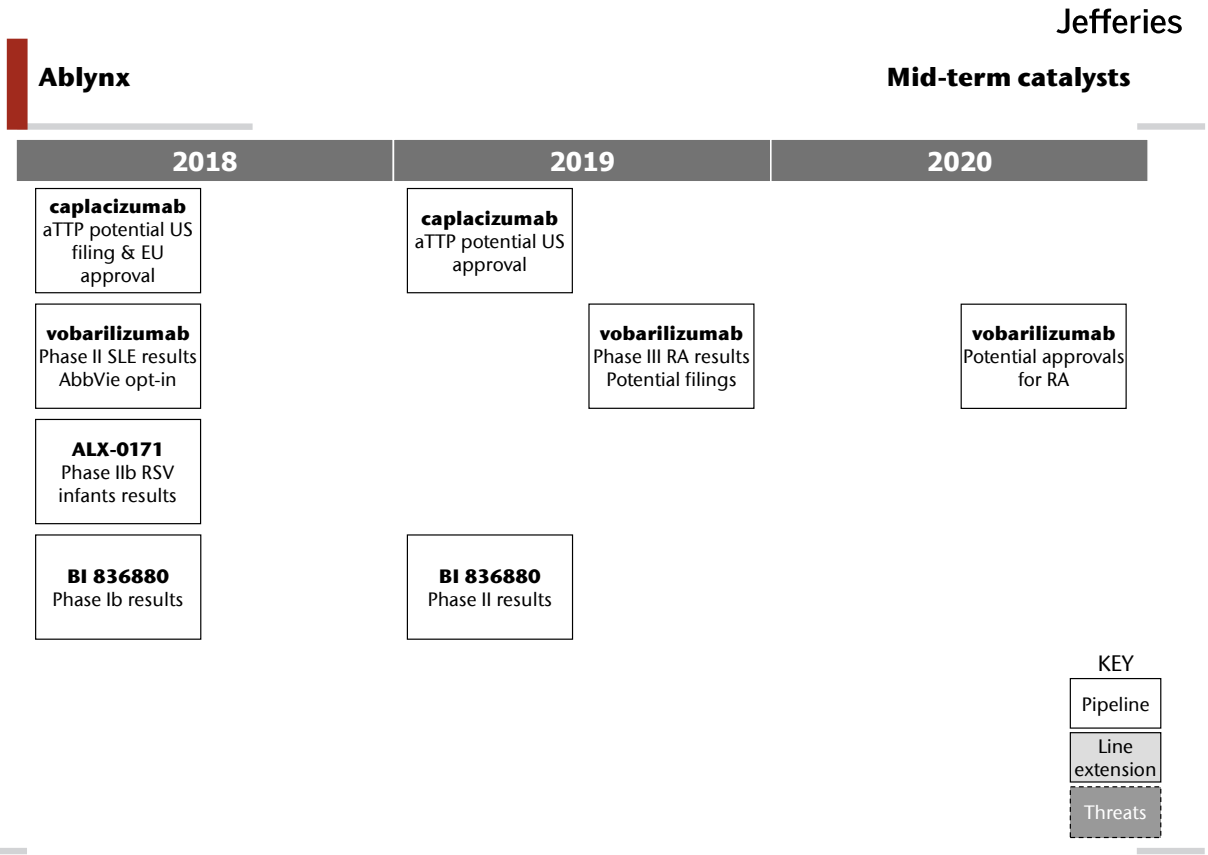
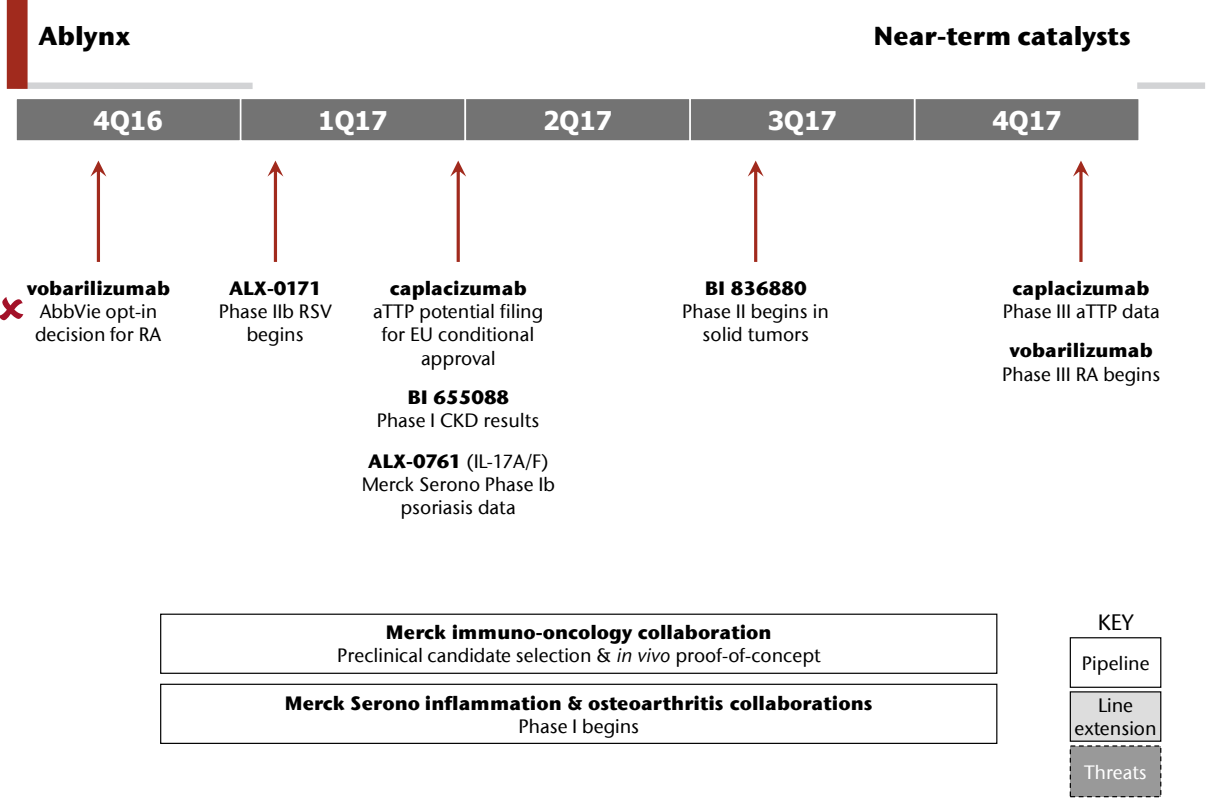
Company	Effective	Product	% increase
Actelion	19/12/2016	Tracleer	+8.0%
		Opsumit	+9.9%
		Valchlor	+6.0%
Almirall	01/01/2017	Acticlate	+9.0%
		Cordran	+4.9%
		Xolegel	+7.9%
		Fluoroplex	+7.9%
		Verdeso	+7.9%
Ipsen	29/12/2016	Somatuline LAR	+2.0%
	15/12/2016	Nutropin AQ	+9.0%
Lundbeck	01/01/2017	Abilify Maintena	+4.5%
Shire	01/01/2017	Vyvanse	+9.0%
		Pentasa	+6.0%
		Lialda	+9.0%
UCB	01/01/2017	Keppra and Keppra XR	+5.0%
		Cimzia	+4.8%
		Vimpat	+9.9%
		Neupro	+9.9%

Source: Jefferies and PriceRx as of 3 January 2017

2017 Catalyst Calendars

Our catalyst charts highlight potential upcoming share price triggers for the stocks under coverage. We have included both biotech and the larger biopharma companies.

Exhibit 1: Ablynx catalysts

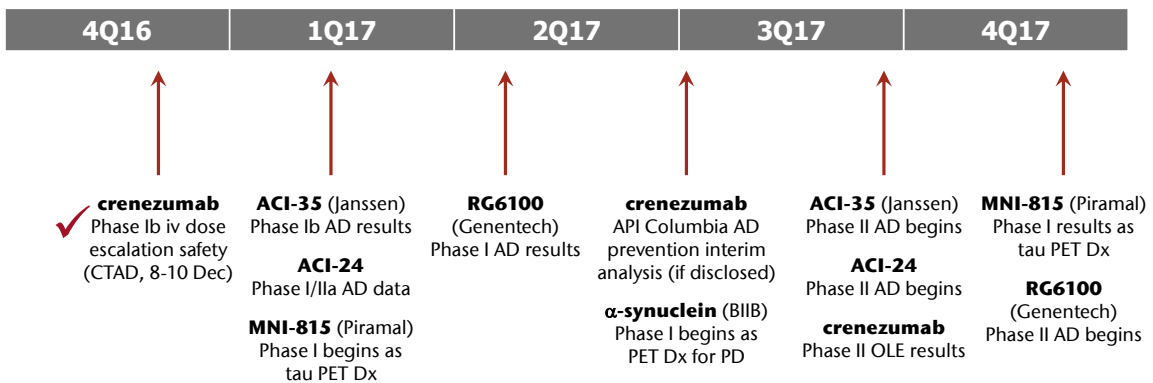


Source: Jefferies

Exhibit 2: AC Immune catalysts

AC Immune

Near-term catalysts



solanezumab (LLY)
Phase III AD results

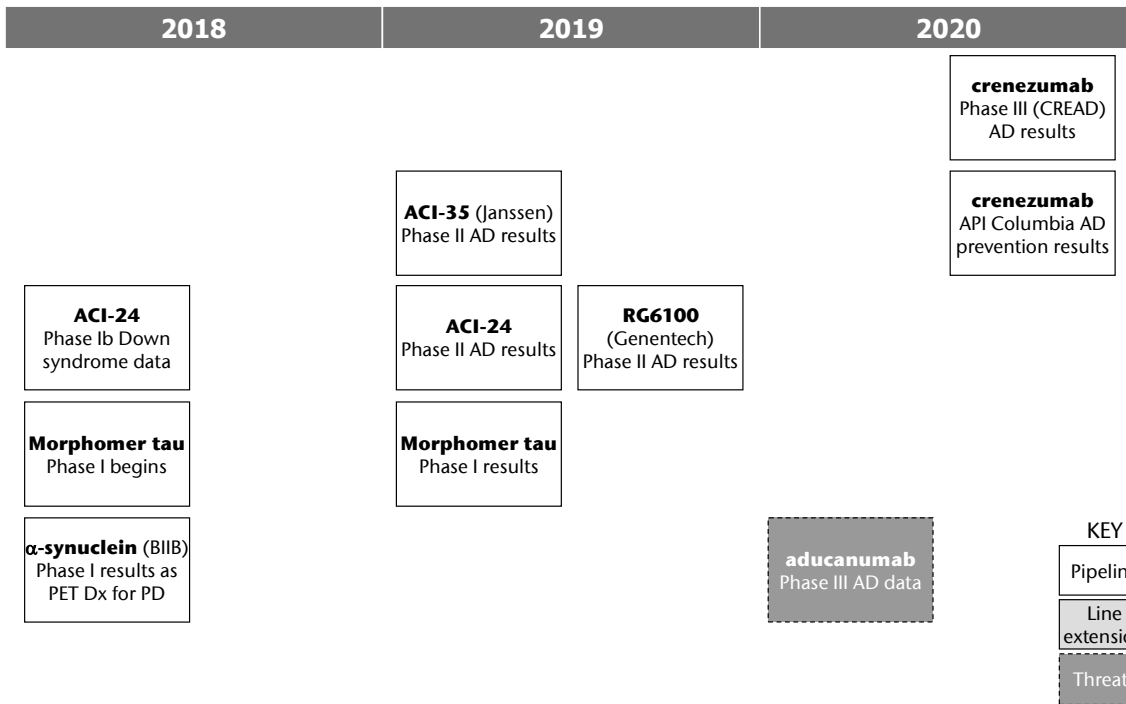
Morphomer and SupraAntigen platforms
Potential collaborations and out-licensing deals for therapeutics and/or diagnostics

KEY

- Pipeline
- Line extension
- Threats

AC Immune

Mid-term catalysts



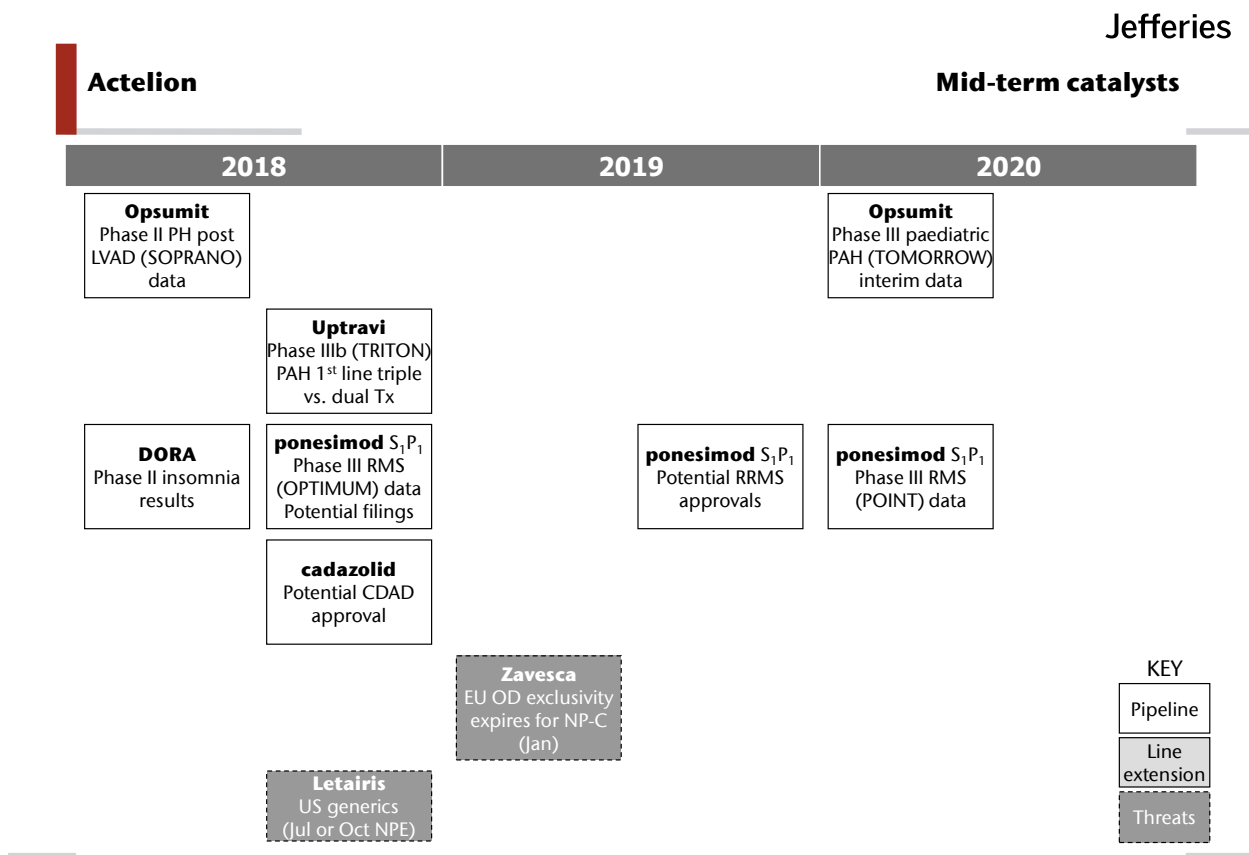
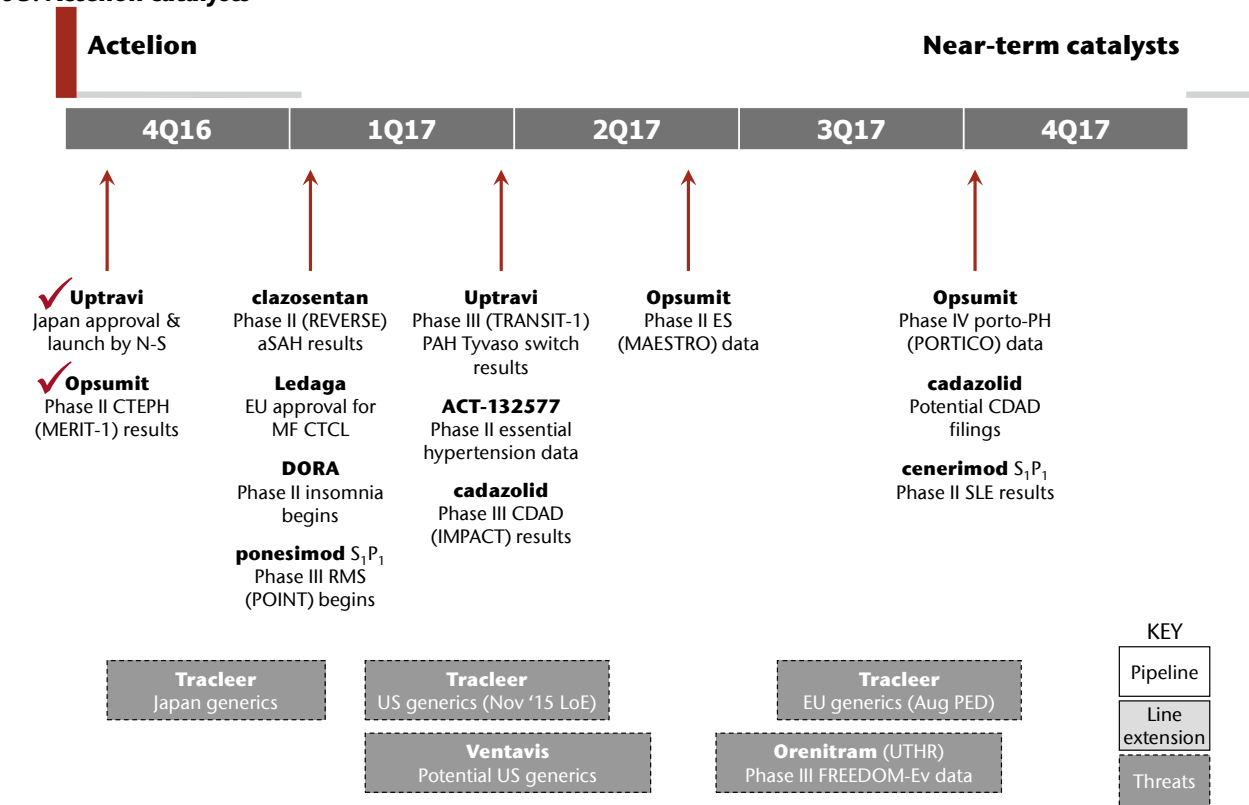
KEY

- Pipeline
- Line extension
- Threats

Jefferies

Source: Jefferies

Exhibit 3: Actelion catalysts



Source: Jefferies