ASTRAZENECA PLC (ADR)

EQUITY RESEARCH

January 13, 2020
Price: $49.85 (01/10/2020)
Price Target: $55.00

OUTPERFORM (1)

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Key Data

Symbol	NYSE: AZN
52-Week Range:	$51.23 - $35.30
Market Cap:	$130.8B
Net Debt (MM):	$12,600.0
Cash/Share:	NA
Dil. Shares Out (MM):	2,624.3
Enterprise Value (MM):	$144,410.2
BV/Share:	NA
Dividend:	$0.90
Yield:	1.81%

FY (Dec)	2018A	2019E	2020E
EPS			
Q1	$0.48	$0.89A	$0.93
Prior Q1	-	-	*$0.95*
Q2	$0.69	$0.73A	$0.96
Prior Q2	-	-	*$0.98*
Q3	$0.71	$0.99A	$1.10
Prior Q3	-	-	*$1.12*
Q4	$1.58	$1.04	$1.16
Prior Q4	-	*$0.99*	*$1.15*
Year	$3.46	$3.65	$4.15
Prior Year	-	*$3.60*	*$4.20*

Reflects updated definition of core financial measures to exclude all intangible asset amortization charges and impairments, except those for IS-related intangibles.

Revenue (MM)			
Year	$22,090.0	$24,405.0	$26,735.0
Prior Year	-	*$24,295.0*	*$26,900.0*

PROMISING NEW PRODUCTS POISED TO DELIVER GROUP-LEADING GROWTH

THE COWEN INSIGHT

AZN has promising new products/pipeline and participates in many large, high growth markets. These prospects could be further strengthened through business development/ partnering. EPS growth looks to be among the best in the industry, with upside possible should its 2023 guidance/ambitions be delivered. AZN's progressive dividend policy is intact and its outlook is one of the strongest in pharma.

EPS Estimated At +5% In 2019, Then Ramps To +14-24% In 2020-25

We estimate 2019 EPS to increase 5%, to $3.65, on revenues of $24.4B (+10%). We estimate an acceleration to strong 14-24% gains in 2020-2025, assuming pipeline delivers and no greater-than-expected discretionary spending. 2018-25 EPS CAGR is forecast at 15%, well above the industry average.

Much Imfinzi Data In 2020

PACIFIC data in unresectable Stage III NSCLC has led to continued Imfinzi sales growth since its U.S. approval in February 2018; strong ROW growth may be boosted by recent China approval. In metastatic NSCLC, POSEIDON posted positive PFS, but we await OS for the Imfinzi+treme+chemo triplet; data in 2020. Priority review for CASPIAN should see Imfinzi approved in 1L SCLC in the first half. Other key catalysts include HIMALAYA (1L HCC) and AEGEAN (adjuvant NSCLC) readouts. AZN 2025 WW PD-(L)1 share is projected to grow to 10% (from ~7% in 2019). We estimate Imfinzi sales at $1.5B in 2019 and $4.7B in 2025.

Tagrisso And Lynparza Have Big Potential; Other New Agents Rolling Out

FLAURA data establishes Tagrisso as the 1L standard in EGFR mutant lung cancer; 2025 sales estimated at $8.65B. The Merck collaboration for Lynparza brought upfront funds and is expanding indications to likely include pancreatic cancer and prostate cancer; 2025 sales estimated at $4B. Calquence (a 55% stake acquired from Acerta) was initially approved for MCL, but recently for CLL with impressive data; 2025 sales estimated at $4.1B. Fasenra, anti IL-5 for asthma, is enjoying a strong rollout; 2025 sales estimated at $2.4B. In 2019 AZN established a partnership with Daiichi Sankyo for trastuzumab deruxtecan which is in late stage trials for breast cancer and other HER2+ tumors; collaboration revenue estimated at $585MM in 2025.

Long-Range Revenue Targets Within Reach

Astra's 10-year plan included sizable revenue expectations such as annual revenue of $45B + by 2023 or $40B when factoring currency; we are at $36.4B. This top-line growth is expected to be driven by a growing and accelerating mid-late stage pipeline (accounting for one-third of the 2023 total), with the remainder due to growth from Brilinta, diabetes, respiratory, emerging markets, and Japan. Core therapeutic areas will be strengthened through partnering and bolt-on acquisitions; management believes a large, transformative transaction is not required.

AstraZeneca Key Upcoming Events

Time Frame	Event Type	Product	Event
2020	Clinical	Breztri (PT010, triple)	Full Ph III data (ETHOS) in COPD exacerbations; positive top-line Aug '19
		Brilinta	Phase III data (THALES) in stroke patients
		Epanova	Phase III data in hypertriglyceridema CVOT
		Fasenra	Phase III data in nasal polyposis
		Imfinzi	Phase III data in neo-adjuvant NSCLC (AEGEAN)
			Phase III data in unresectable Stage III NSCLC (PACIFIC-2)
		Imfinzi + tremelimumab	Phase III data in 1L SSCHN (KESTREL)
			Phase III data (DANUBE) 1L bladder cancer
			Phase III data in liver cancer (HIMALAYA)
			Full Ph III data (NEPTUNE) in 1L NSCLC; missed OS Aug '19
			Phase III data (POSEIDON) in 1L NSCLC; positive top-line Oct '19
		Lynparza + cediranib	Phase III data in 2L ovarian cancer
		PT027	Phase III data in asthma
		Roxadustat	Phase III data in anemia of myelodysplastic syndrome
		Tezepelumab	Phase III data in severe asthma
		Trastuzumab deruxtecan (DS-8201)	Phase III data in 3L, HER2+ gastric cancer
	Regulatory	Anifrolumab	Regulatory filings in SLE; H2:20
		Breztri	EU approval, U.S. re-filing/approval in COPD
		Brilinta	Regulatory filings in stroke patients (THALES)
			U.S. approval in high-risk T2DM/CAD (THEMIS-PCI)
		Calquence	EU/JP filings in CLL
		Enhertu	JP approval in 3L+ HER2+ mBC
		Fasenra	Regulatory filings in nasal polyposis
		Farxiga	U.S. approval/EU filing for HF CV outcomes; PDUFA Q2:20
			CN approval for T2DM CV outcomes
		Imfinzi + chemo	U.S. approval in 1L SCLC (CASPIAN); PDUFA Q1:20
		Imfinzi + tremelimumab	Regulatory filings in 1L bladder cancer (DANUBE)
			Regulatory filings in 1L SSCHN (KESTREL)
			Regulatory filings in 1L NSCLC (POSEIDON)
		Lokelma	JP approval for hyperkalemia
		Lynparza (w/MRK)	CN approval in BRCAm breast cancer
			U.S./EU filings for 1L ovarian maintenance cancer (PAOLA-1)
			U.S./EU filings for BRCA/ATM 2L mCRPC (PROfound)
			U.S. filing for 3L BRCAm ovarian cancer
		Lynparza + cediranib	Regulatory filings in 2L ovarian cancer
		Roxadustat	U.S. approval for anemia
		Selumetinib (w/MRK)	EU filing in neurofibromatosis type 1
			U.S. approval in neurofibromatosis type 1; PDUFA Q2:20
		Symbicort	EU/CN filing for mild asthma

Source: Company data

EPS Recovery Starts 2019; Standout Growth Thereafter

Recovery Underway In 2019 With EPS +5%

We estimate EPS to increase 5% in 2019, to $3.65, driven by a 10% increase in revenue to $24.405B. We assume collaboration revenue of $805MM (-23%). GPM is estimated to increase 0.5pp to 80%. SG&A is estimated to increase 1%, R&D to remain flat, and other operating income decrease by $737MM to $1,410MM, leading to a 1.8pp increase in operating margin to 27.5%. We expect the tax rate to increase 9.1pp to 20.5% and shares to increase by 34MM to 1,301MM.

Astra 2019 Guidance Versus Cowen Estimates

	AZN Guidance *	Our Estimates **
Product Sales	**Low-to-mid-teens increase at CER**	$23.6B (+12%)
Collaboration Revenue + Other Income (net)	Lower than 2018 (of $3,188MM)	$2,215MM
Core Operating Expense	Low single digit % increase at CER	+1%
Core Operating Profit	**Increase ahead of product sales**	+18%
Tax Rate	**20-22%**	20.5%
Core EPS	$3.50-3.70 at CER	$3.65

* Assuming Fx rates through SEptember 2019, low single digit negative impact on sales and EPS
** includes Fx impact
Bold=revised

Source: Cowen and Company, AstraZeneca

2020 EPS Growth Estimated To Accelerate To +14%

We estimate 2020 EPS at $4.15 (+14%), on a 10% increase in revenue to $26.7B. We assume collaboration revenue of $510MM (-37%). GPM is estimated to increase 0.3pp to 80.3%. SG&A is estimated to increase 5%, R&D to increase 4%, and other operating income decline by $510MM to $900MM, leading to a 0.4pp increase in operating margin to 27.9%. The tax rate is estimated to decrease 0.5pp to 20% and shares to increase 11MM to 1,312MM.

14-24% EPS Gains On Tap For 2021-2025

EPS are projected to grow +14-24% annually 2021-25 led by 8-14% top-line gains. Collaboration revenue is estimated to increase by $10-40MM each year 2021-25, in part due to AZN territory profit from the trastuzumab collaboration with Daiichi. We look for gross P.M. to increase 0.2-0.3pp each year 2021-25, R&D to increase 4-8% 2021-25, and SG&A to increase 3-10% each year 2021-25. We estimate other operating income to decline $100MM each year 2021-25; the tax rate to hold at 20%; and the share count to remain at 1,312MM. We forecast EPS of $9.20 in 2025.

Long-Range Strategic Plan Portrays Lofty Growth Expectations

Management forecasts annual revenue of $45B+ by 2023 or $40B when factoring in currency (our estimate is $36.4B). This top-line growth is expected to be driven by a growing and accelerating mid- to late-stage pipeline including: oncology agents Imfinzi (PD-L1; approved for 2L bladder (US) and unresectable Stage III NSCLC (U.S.,EU, and China), Tagrisso (EGFR; approved in U.S., EU, and China), Lynparza (PARP; approved U.S.,EU, Japan, China); respiratory agents Bevespi (LABA/LAMA; U.S. approved), PT010 (LABA/LAMA/ICS; U.S./EU approvals expected 2020) and Fasenra (asthma; U.S., EU approved); and diabetes combo saxagliptin/ dapagliflozin (Qtern, approved 2017). Pipeline products are expected to account for one-third of the 2023 total, with the remainder due to growth from key platforms: Brilinta, diabetes, respiratory, emerging markets, and Japan.

Management estimates risk-adjusted peak year sales for pipeline products to be $23B; non-risk adjusted estimated at $63B. Probability of success for the overall portfolio is 36%, with some drugs given a much lower probability.

Balance Sheet Supports Dividend, Other Needs

As of Q3:19, Astra had cash/equivalents and short-term investments of $4B, short-term debt of $0.2B, and long-term debt of $17.2B. We estimate free cash flow (operating CF minus capex) to be $2.4B for 2019, increasing annually over the next five years to approximately $12B+ in 2025, supporting annual dividend payments of $3.5-4B.

Speculation On 2019-2025 EPS Outcomes ($MM)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comments
Tagrisso	$0.35	$0.59	$0.83	$1.04	$1.20	$1.35	$1.51	$1.66	55%	25%	EGFRm+; T790M+ NSCLC 1st line; solid tumors in Phase I; $4B potential in G7 countries
Imfinzi	0.12	0.27	0.40	0.55	0.66	0.73	0.82	0.91	85%	34%	Durvalumab; PD-L1; Ph III in SCCHN, lung and H&N w/treme, other solid tumors
Lynparza	0.12	0.22	0.31	0.41	0.50	0.59	0.69	0.78	61%	31%	Olaparib; oral PARP-BRCA; ovarian, breast, gastric, prostate, pancreatic; collaboration with MRK
Roxadustat	0.00	0.00	0.04	0.11	0.15	0.20	0.25	0.30	NM	NM	Hypoxia-induced factor prolyl hydroxylase inhibitors; anemia in CKD/ESRD; NDA US (H2:19), China apprv'd 12/18
Brilinta	0.25	0.29	0.31	0.33	0.35	0.36	0.34	0.29	12%	2%	Reversible ADP rec. antag; oral; arterial thrombosis; ACS apprd; $2B potential, down from $4B, given trial failures
Symbicort	0.48	0.44	0.40	0.37	0.33	0.30	0.26	0.22	-8%	-10%	4.1% market share in U.S. 11/19; stable volume but price pressure
Nexium	0.32	0.26	0.24	0.22	0.22	0.21	0.20	0.20	-13%	-6%	Generics launched 2/15
Crestor	0.27	0.24	0.21	0.19	0.17	0.15	0.14	0.12	-10%	-10%	Patent exp. 7/16 (with pedi exclusivity) US, numerous generics lanched; 6/17 EU, LOE in Canada
Arimidex	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.05	2%	2%	Estrogen antagonist, breast cancer; generics eroding franchise
Other New Drugs	0.35	0.48	0.66	0.93	1.19	1.46	1.84	2.19	37%	30%	Fasenra, Calquence, Tudorza, tremelimumab, Lokelma, many others
Diabetes Franchise	0.49	0.50	0.52	0.54	0.57	0.59	0.62	0.65	3%	4%	Onglyza, Forxiga, Bydureon, Byetta; BMY's 50% stake purchased Q1:14
Other	0.70	0.31	0.19	0.43	0.73	1.05	1.40	1.83	-47%	15%	
EPS	**$3.46**	**$3.65**	**$4.15**	**$5.15**	**$6.10**	**$7.05**	**$8.10**	**$9.20**	**10%**	**15%**	**Versus industry averages of +9% and +9%**
% Change	-19%	5%	14%	24%	18%	15%	15%	14%			

Source: Company data, Cowen and Company

AstraZeneca Quarterly Core EPS

	Product Sales	Collaboration Revenue (1)	Total Revenue	% Chg.	Gross P.M. (reported)	SG&A $MM	SG&A % Sls	R&D $MM	R&D % Sls	Other Op. Inc. (2)	Op. P.M.	Pretax P.M.	Tax Rate	Net Income	EPS (Dil.)	Y/Y % Chg.	Shares (MM)
Q1	$4,985	$193	$5,178	-4%	78.8%	$2,028	39.2%	$1,240	23.9%	$124	17.3%	13.7%	17.9%	$603	$0.48	-52%	1,266
Q2	5,030	125	5,155	2%	81.3%	2,126	41.2%	1,318	25.6%	580	24.5%	20.3%	19.5%	875	0.69	-21%	1,267
Q3	5,266	74	5,340	-14%	79.4%	2,061	38.6%	1,242	23.3%	439	24.7%	20.3%	19.7%	894	0.71	-37%	1,267
Q4	5,768	649	6,417	11%	78.6%	2,436	38.0%	1,466	22.8%	1,004	34.2%	30.9%	0.2%	2,002	1.58	21%	1,267
2018	**$21,049**	**$1,041**	**$22,090**	**-2%**	**79.5%**	**$8,651**	**39.2%**	**$5,266**	**23.8%**	**$2,147**	**25.7%**	**21.8%**	**11.4%**	**$4,374**	**$3.46**	**-19%**	**1,267**
Q1	$5,465	$26	$5,491	6%	80.5%	$2,066	37.6%	$1,225	22.3%	$594	30.0%	26.1%	23.1%	$1,132	0.89	88%	1,267
Q2	5,718	105	5,823	13%	82.1%	2,192	37.6%	1,280	22.0%	114	23.4%	19.4%	17.9%	953	0.73	5%	1,311
Q3	6,132	274	6,406	20%	79.4%	2,206	34.4%	1,321	20.6%	352	29.3%	25.8%	23.1%	1,292	0.99	40%	1,312
Q4E	6,275	400	6,675	4%	78.2%	2,276	34.1%	1,464	21.9%	350	27.3%	24.1%	17.3%	1,364	1.04	-34%	1,312
2019E	**$23,600**	**$805**	**$24,405**	**10%**	**80.0%**	**$8,740**	**35.8%**	**$5,290**	**21.7%**	**$1,410**	**27.5%**	**23.9%**	**20.5%**	**$4,741**	**$3.65**	**5%**	**1,301**
Q1E	$6,115	$100	$6,215	13%	80.8%	$2,190	35.2%	$1,275	20.5%	$200	27.3%	23.9%	20.0%	$1,220	0.93	4%	1,312
Q2E	6,215	150	6,365	9%	82.4%	2,315	36.4%	1,330	20.9%	200	27.3%	24.2%	20.0%	1,262	0.96	32%	1,312
Q3E	6,780	165	6,945	8%	79.6%	2,330	33.5%	1,370	19.7%	200	28.4%	25.5%	20.0%	1,448	1.10	12%	1,312
Q4E	7,045	150	7,195	8%	78.6%	2,325	32.3%	1,520	21.1%	300	28.4%	25.9%	20.0%	1,518	1.16	11%	1,312
2020E	**$26,225**	**$510**	**$26,735**	**10%**	**80.3%**	**$9,160**	**34.3%**	**$5,495**	**20.6%**	**$900**	**27.9%**	**24.9%**	**20.0%**	**$5,448**	**$4.15**	**14%**	**1,312**
Q1E	$7,010	$80	$7,090	77%	81.1%	$2,410	34.0%	$1,375	19.4%	$175	29.2%	26.5%	20.0%	$1,532	1.17	26%	1,312
Q2E	7,145	130	7,275	77%	82.6%	2,535	34.8%	1,435	19.7%	175	29.6%	27.0%	20.0%	1,602	1.22	27%	1,312
Q3E	7,720	145	7,865	77%	80.0%	2,555	32.5%	1,475	18.8%	175	30.2%	27.9%	20.0%	1,784	1.36	23%	1,312
Q4E	8,035	130	8,165	77%	78.8%	2,575	31.5%	1,625	19.9%	275	29.9%	27.7%	20.0%	1,842	1.40	21%	1,312
2021E	**$29,840**	**$555**	**$30,395**	**14%**	**80.6%**	**$10,075**	**33.1%**	**$5,910**	**19.4%**	**$800**	**29.7%**	**27.3%**	**20.0%**	**$6,760**	**$5.15**	**24%**	**1,312**
2022P	**$33,010**	**$565**	**$33,575**	**10%**	**80.8%**	**$10,770**	**32.1%**	**$6,250**	**18.6%**	**$700**	**31.4%**	**29.4%**	**20.0%**	**$8,004**	**$6.10**	**18%**	**1,312**
2023P	**$35,815**	**$595**	**$36,410**	**8%**	**81.0%**	**$11,270**	**31.0%**	**$6,500**	**17.9%**	**$600**	**33.1%**	**31.3%**	**20.0%**	**$9,244**	**$7.05**	**15%**	**1,312**
2024P	**$39,090**	**$625**	**$39,715**	**9%**	**81.2%**	**$12,025**	**30.3%**	**$6,750**	**17.0%**	**$500**	**34.5%**	**33.1%**	**20.0%**	**$10,624**	**$8.10**	**15%**	**1,312**
2025P	**$42,055**	**$660**	**$42,715**	**8%**	**81.4%**	**$12,400**	**29.0%**	**$7,000**	**16.4%**	**$400**	**36.2%**	**35.0%**	**20.0%**	**$12,076**	**$9.20**	**14%**	**1,312**

(1) Divestitures where some interest is retained

(2) Divestitures where no interest is retained; payments to BMY for diabetes products (no impact on core EPS)

Source: Company data, Cowen and Company estimates

AstraZeneca Quarterly Product Line Buildup ($MM)

	Q1:18	Q2:18	Q3:18	Q4:18	2018	Q1:19	Q2:19	Q3:19	Q4:19E	2019E	Q1:20E	Q2:20E	Q3:20E	Q4:20E	2020E	Q1:21E	Q2:21E	Q3:21E	Q4:21E	2021E
Nexium - U.S.	$100	$87	$62	$57	$306	$66	$53	$56	$50	$225	$45	$40	$35	$30	$150	$25	$20	$15	$10	$70
Nexium - E.U. (lc, ex fx)																				
Nexium - E.U.	61	61	57	56	235	16	16	17		50										
Nexium - Estab. ROW	105	133	122	111	471	91	145	96	90	420	80	135	85	80	380	70	125	75	70	340
Nexium - Emerging ROW	182	161	181	166	690	190	179	205	175	750	195	185	210	180	770	200	190	215	185	790
Nexium - Worldwide	448	442	422	390	1,702	363	393	374	315	1,445	320	360	330	290	1,300	295	335	305	265	1,200
Losec - U.S.	$1	$3	$1	$2	$7	$1	$3	$3	$0	$5	$5	$0	$0	$0	$5	$5	$0	$0	$0	$5
Losec - E.U. (lc, ex fx)									5		0	0	0	0		0	0	0	0	
Losec - E.U.	16	20	15	19	70	18	13	14	5	50	0	0	0	0	0	0	0	0	0	0
Losec - Estab. ROW	6	11	8	9	34	6	7	7	5	25	5	5	5	0	15	5	5	0	0	10
Losec - Emerging ROW	46	42	43	30	161	51	45	49	35	180	55	50	55	40	200	60	55	60	45	220
Losec - Worldwide	69	76	67	60	272	76	68	73	45	260	65	55	60	40	220	70	60	60	45	235
Movantik/Moventig	28	24	32	25	109	25	22	25	25	95	25	25	20	20	90	25	20	20	20	85
Axanum	0	-1	-1	-1	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gastrointestinal	**$545**	**$541**	**$520**	**$474**	**$2,080**	**$464**	**$483**	**$472**	**$385**	**$1,800**	**$410**	**$440**	**$410**	**$350**	**$1,610**	**$390**	**$415**	**$385**	**$330**	**$1,520**
% Change	-3%	-22%	-8%	-9%	-11%	-15%	-11%	-9%	-19%	-13%	-12%	-9%	-13%	-9%	-11%	-5%	-6%	-6%	-6%	-6%
Crestor - U.S.	$46	$44	$38	$42	$170	$26	$28	$34	$30	$120	$15	$15	$25	$25	$80	$15	$15	$15	$15	$60
Crestor - E.U. (lc, ex fx)									35		30	30	30	25		25	25	20	15	
Crestor - E.U.	65	46	48	44	203	39	36	37	35	145	30	30	30	25	115	25	25	20	15	85
Crestor - Estab. ROW	40	62	60	57	219	45	64	53	50	210	35	55	45	40	175	25	45	35	30	135
Crestor - Emerging ROW	238	186	207	210	841	225	182	214	220	840	215	170	205	210	800	205	160	195	200	760
Crestor - Worldwide	389	338	353	353	1,433	335	310	338	335	1,320	295	270	305	300	1,170	270	245	265	260	1,040
Seloken/Toprol XL - U.S.	$18	$8	$7	$6	$39	$23	$3	$4	$5	$35	$10	$10	$5	$5	$30	$10	$5	$5	$5	$25
Seloken/Toprol XL - E.U. (lc, ex fx)									0		5	5	5	0		5	5	0	0	
Seloken/Toprol XL - E.U.	6	6	4	3	19	6	7	5	0	20	5	5	5	0	15	5	5	0	0	10
Seloken/Toprol XL - Estab. ROW	3	4	3	3	13	3	2	3	0	10	0	5	0	0	5	0	5	0	0	5
Seloken/Toprol XL - Emerging ROW	173	155	165	148	641	193	156	164	155	670	205	165	175	165	710	215	175	185	175	750
Seloken/Toprol XL - Worldwide	200	173	179	160	712	225	168	176	160	730	220	185	185	170	760	230	190	190	180	790
Atacand - U.S.	$7	$3	$1	$2	$13	$2	$4	$2	$0	$10	$5	$0	$0	$0	$5	$5	$0	$0	$0	$5
Atacand - E.U. (lc, ex fx)																				
Atacand - E.U.	22	19	21	8	70	4	11	7		20										
Atacand - Estab. ROW	5	5	5	5	20	5	4	5	0	15	5	5	0	0	10	5	0	0	0	5
Atacand - Emerging ROW	37	39	38	43	157	39	37	41	40	155	30	30	35	35	130	25	25	30	30	110
Atacand - Worldwide	71	66	65	58	260	50	56	55	40	200	40	35	35	35	145	35	25	30	30	120

Source: Company data, Cowen and Company estimates

AstraZeneca Quarterly Product Line Buildup ($MM) (continued)

	Q1:18	Q2:18	Q3:18	Q4:18	2018	Q1:19	Q2:19	Q3:19	Q4:19E	2019E	Q1:20E	Q2:20E	Q3:20E	Q4:20E	2020E	Q1:21E	Q2:21E	Q3:21E	Q4:21E	2021E
Onglyza - U.S.	$49	$49	$64	$61	$223	$78	$42	$54	$50	$225	$70	$35	$45	$45	$195	$65	$30	$40	$40	$175
Onglyza - E.U. (lc, ex fx)									15		15	15	15	15		15	15	10	10	
Onglyza - E.U.	23	24	21	21	89	19	17	17	15	70	15	15	15	15	60	15	15	10	10	50
Onglyza - Estab. ROW	17	12	15	15	59	13	13	12	15	55	10	10	15	15	50	10	10	10	15	45
Onglyza - Emerging ROW	40	41	40	51	172	43	44	44	55	185	40	40	40	50	170	35	35	35	45	150
Onglyza - Worldwide	129	126	140	148	543	153	116	127	135	530	135	100	115	125	475	125	90	95	110	420
Brilinta - U.S.	$115	$144	$152	$177	$588	$153	$168	$179	$195	$695	$175	$190	$200	$215	$780	$195	$210	$220	$235	$860
Brilinta - E.U. (lc, ex fx)									95		90	95	100	105		100	105	110	115	
Brilinta - E.U.	86	86	85	91	348	83	88	91	95	355	90	95	100	105	390	100	105	110	115	430
Brilinta - Estab. ROW	16	14	15	14	59	15	13	15	15	60	20	15	15	15	65	20	15	15	20	70
Brilinta - Emerging ROW	76	72	84	94	326	97	120	131	130	480	90	110	120	120	440	80	100	110	110	400
Brilinta - Worldwide	293	316	336	376	1,321	348	389	416	435	1,590	375	410	435	455	1,675	395	430	455	480	1,760
Bydureon - U.S.	$111	$123	$126	$115	$475	$117	$117	$106	$110	$450	$110	$110	$110	$115	$445	$115	$115	$115	$120	$465
Bydureon - E.U. (lc, ex fx)									20		20	15	20	20		20	20	20	20	
Bydureon - E.U.	23	20	19	19	81	18	16	16	20	70	20	15	20	20	75	20	20	20	20	80
Bydureon - Estab. ROW	5	5	5	5	20	5	3	3	5	15	5	5	5	5	20	5	5	5	10	25
Bydureon - Emerging ROW	0	7	2	-1	8	2	5	2	0	10	0	5	5	5	15	5	5	5	5	20
Bydureon - Worldwide	139	155	152	138	584	142	141	127	135	545	135	135	140	145	555	145	145	145	155	590
Byetta - U.S.	$15	$17	$23	$19	$74	$20	$15	$17	$15	$65	$15	$10	$15	$15	$55	$10	$10	$10	$15	$45
Byetta - E.U. (lc, ex fx)									5		5	5	5	0		5	5	0	0	
Byetta - E.U.	7	9	6	7	29	6	4	4	5	20	5	5	5	0	15	5	5	0	0	10
Byetta - Estab. ROW	4	4	3	4	15	3	3	3	5	15	0	5	0	5	10	0	5	0	0	5
Byetta - Emerging ROW	5	-1	2	2	8	1	3	4	0	10	0	5	5	0	10	0	5	5	0	10
Byetta - Worldwide	31	29	34	32	126	30	25	28	25	110	20	25	25	20	90	15	25	15	15	70
Farxiga - U.S.	$127	$139	$154	$171	$591	$131	$139	$126	$150	$545	$140	$140	$140	$155	$575	$145	$150	$145	$165	$605
Forxiga - E.U. (lc, ex fx)									95		100	100	105	105		110	110	115	115	
Forxiga - E.U.	74	78	79	84	315	89	89	95	95	370	100	100	105	105	410	110	110	115	115	450
Forxiga - Estab. ROW	29	35	37	48	149	34	38	43	50	165	40	40	45	55	180	45	45	50	60	200
Forxiga - Emerging ROW	69	88	85	94	336	95	111	133	135	475	110	125	150	150	535	125	140	160	160	585
Farxiga - Worldwide	299	340	355	397	1,391	349	377	397	430	1,555	390	405	440	465	1,700	425	445	470	500	1,840
Others - U.S.	$5	$1	$0	$1	$5	$1	$2	$1	$5	$5	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Others - E.U. (lc, ex fx)									15		15	15	15	15		15	15	10	10	
Others - E.U.	15	18	10	18	61	19	15	19	15	70	15	15	15	15	60	15	15	10	10	50
Others - Estab. ROW	4	7	10	6	27	3	7	6	5	20	0	5	5	5	15	0	0	5	5	10
Others - Emerging ROW	61	69	53	50	233	52	43	45	40	180	45	40	40	35	160	40	35	35	30	140
Others - Worldwide	85	93	73	75	326	75	63	71	65	275	60	60	60	55	235	55	50	50	45	200

Source: Company data, Cowen and Company estimates

AstraZeneca Quarterly Product Line Buildup ($MM) (continued)

	Q1:18	Q2:18	Q3:18	Q4:18	2018	Q1:19	Q2:19	Q3:19	Q4:19E	2019E	Q1:20E	Q2:20E	Q3:20E	Q4:20E	2020E	Q1:21E	Q2:21E	Q3:21E	Q4:21E	2021E
Lokelma						5	5	4	5	20	5	5	10	10	30	10	10	15	15	50
Epanova																		20	30	50
Cotadutide																				
MEDI5884																				
MEDI6012																				
AZN5718																				
AZN8601																				
AZN4831																				
Symlin	9	7	8	10	34	7	8	10	10	35	10	10	10	10	40	10	10	10	15	45
Cardiovascular	**$1,645**	**$1,643**	**$1,695**	**$1,747**	**$6,730**	**$1,719**	**$1,658**	**$1,749**	**$1,775**	**$6,910**	**$1,685**	**$1,640**	**$1,760**	**$1,790**	**$6,875**	**$1,715**	**$1,665**	**$1,760**	**$1,835**	**$6,975**
% Change	-7%	-7%	-4%	-10%	-7%	4%	1%	3%	2%	3%	-2%	-1%	1%	1%	-1%	2%	2%	0%	3%	1%
Fasenra - U.S.	$19	$48	$62	$89	$218	$93	$115	$135	$145	$490	$155	$165	$175	$185	$680	$195	$205	$215	$225	$840
Fasenra - E.U. (lc, ex fx)									40		40	40	45	45		55	60	65	70	
Fasenra - E.U.	2	6	9	15	32	18	27	36	40	120	40	40	45	45	170	55	60	65	70	250
Fasenra - Estab. ROW	0	11	15	20	46	18	24	28	35	105	40	45	50	55	190	60	65	65	70	260
Fasenra - Emerging ROW	0	0	0	1	1	0	1	3	5	10	5	5	5	5	20	10	10	10	10	40
Fasenra - Worldwide	21	65	86	125	297	129	167	202	225	725	240	255	275	290	1,060	320	340	355	375	1,390
Symbicort - U.S.	$183	$256	$216	$207	$862	$176	$206	$203	$190	$775	$150	$175	$175	$150	$650	$125	$150	$150	$125	$550
Symbicort - E.U. (lc, ex fx)									160		155	145	135	140		130	120	110	115	
Symbicort - E.U.	212	199	177	185	773	182	172	154	160	670	155	145	135	140	575	130	120	110	115	475
Symbicort - Estab. ROW	111	104	103	113	431	94	77	118	120	410	85	70	110	110	375	75	60	100	100	335
Symbicort - Emerging ROW	128	113	123	131	495	133	130	138	140	540	145	140	150	150	585	155	150	160	160	625
Symbicort - Worldwide	634	672	619	636	2,561	585	585	613	610	2,395	535	530	570	550	2,185	485	480	520	500	1,985
Pulmicort - U.S.	$29	$30	$22	$35	$116	$24	$32	$33	$30	$120	$20	$30	$30	$25	$105	$15	$25	$25	$20	$85
Pulmicort - E.U. (lc, ex fx)									20		20	20	15	15		15	15	15	15	
Pulmicort - E.U.	27	23	18	22	90	25	19	16	20	80	20	20	15	15	70	15	15	15	15	60
Pulmicort - Estab. ROW	20	22	18	25	85	20	20	20	20	80	20	20	20	15	75	20	20	15	15	70
Pulmicort - Emerging ROW	270	212	206	307	995	314	262	269	325	1,170	335	280	290	345	1,250	355	300	310	365	1,330
Pulmicort - Worldwide	346	287	264	389	1,286	383	333	338	395	1,450	395	350	355	400	1,500	405	360	365	415	1,545
Tudorza/Eklira - U.S.	$11	$18	$1	$3	$25	$2	$2	$1	$5	$5	$5	$0	$0	$0	$5	$5	$0	$0	$0	$5
Tudorza/Eklira - E.U. (lc, ex fx)									20		20	15	20	20		20	20	20	25	
Tudorza/Eklira - E.U.	20	18	16	20	74	16	15	13	20	65	20	15	20	20	75	20	20	20	25	85
Tudorza/Eklira - Estab. ROW	2	4	2	2	10	1	2	1	5	10	0	5	5	5	15	5	5	5	5	20
Tudorza/Eklira - Emerging ROW	1	-1	1	0	1	1	-2	2	5	5	0	0	5	5	10	0	5	5	5	15
Tudorza/Eklira - Worldwide	34	39	18	19	110	20	13	17	35	85	25	20	30	30	105	30	30	30	35	125
Daliresp/Daxas - U.S.	$29	$38	$43	$45	$155	$41	$48	$45	$45	$180	$45	$50	$50	$50	$195	$50	$50	$55	$55	$210
Daliresp/Daxas - E.U. (lc, ex fx)									10		10	5	10	10		10	10	10	10	
Daliresp/Daxas - E.U.	7	7	6	8	28	6	6	7	10	30	10	5	10	10	35	10	10	10	10	40
Daliresp/Daxas - Estab. ROW	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Daliresp/Daxas - Emerging ROW	2	-1	3	1	5	1	1	1	0	5	0	0	5	0	5	0	0	5	0	5
Daliresp/Daxas - Worldwide	38	45	52	54	189	48	56	53	55	210	55	55	65	60	235	60	60	70	65	255
Duaklir - U.S.	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Duaklir - E.U. (lc, ex fx)									20		20	15	20	20		20	20	20	20	
Duaklir - E.U.	27	20	23	21	91	19	17	17	20	75	20	15	20	20	75	20	20	20	20	80
Duaklir - Estab. ROW	1	1	0	1	3	0	1	0	5	5	0	0	5	5	10	0	5	5	5	15
Duaklir - Emerging ROW	0	1	0	0	1	1	-1	1	0	0	0	0	0	0	0	0	0	0	0	0
Duaklir - Worldwide	28	22	23	22	95	20	17	18	25	80	20	15	25	25	85	20	25	25	25	95
Others - U.S.	$5	$0	$0	$3	$2	$0	$1	$1	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Others - E.U. (lc, ex fx)									30		20	20	15	25		20	15	15	25	
Others - E.U.	31	44	33	36	144	19	20	15	30	85	20	20	15	25	80	20	15	15	25	75
Others - Estab. ROW	12	10	15	11	48	1	3	2	5	10	5	5	5	0	15	5	5	5	5	20
Others - Emerging ROW	37	24	22	57	140	68	47	49	60	225	75	50	50	65	240	80	55	55	65	255
Others - Worldwide	75	78	70	107	330	88	71	67	95	320	100	75	70	90	335	105	75	75	95	350

Source: Company data, Cowen and Company estimates

AstraZeneca Quarterly Product Line Buildup ($MM) (continued)

	Q1:18	Q2:18	Q3:18	Q4:18	2018	Q1:19	Q2:19	Q3:19	Q4:19E	2019E	Q1:20E	Q2:20E	Q3:20E	Q4:20E	2020E	Q1:21E	Q2:21E	Q3:21E	Q4:21E	2021E
Bevespi Aerosphere	5	8	10	10	33	10	10	10	15	45	15	20	20	20	75	25	25	30	30	110
Breztri (PT010)								1	5	5	10	10	15	15	50	20	25	25	30	100
PT027																				
Tezepelumab																				
AZN8871																				
Abediterol																				
AZN7594																				
AZN9567																				
AZN1402																				
AZN7986																				
Respiratory	**$1,181**	**$1,216**	**$1,142**	**$1,362**	**$4,901**	**$1,283**	**$1,252**	**$1,319**	**$1,460**	**$5,315**	**$1,395**	**$1,330**	**$1,425**	**$1,480**	**$5,630**	**$1,470**	**$1,420**	**$1,495**	**$1,570**	**$5,955**
% Change	0%	11%	5%	2%	4%	9%	3%	15%	7%	8%	9%	6%	8%	1%	6%	5%	7%	5%	6%	6%
Arimidex - U.S.	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$5	$5	$0	$0	$0	$5	$5
Arimidex - E.U. (lc, ex fx)									5		5	5	5	5		0	5	5	5	
Arimidex - E.U.	8	7	8	8	31	6	9	6	5	25	5	5	5	5	20	0	5	5	5	15
Arimidex - Estab. ROW	11	14	12	12	49	9	15	10	10	45	10	10	10	10	40	10	10	10	5	35
Arimidex - Emerging ROW	35	36	35	26	132	36	36	46	30	150	40	40	45	35	160	45	45	40	40	170
Arimidex - Worldwide	54	57	55	46	212	51	60	62	45	220	55	55	60	55	225	55	60	55	55	225
Casodex - U.S.	$0	$0	$1	$0	$1	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Casodex - E.U. (lc, ex fx)									5		5	5	0	0		5	0	0	0	
Casodex - E.U.	6	5	4	5	20	4	4	4	5	15	5	5	0	0	10	5	0	0	0	5
Casodex - Estab. ROW	15	19	15	18	67	13	19	14	15	60	10	15	10	15	50	10	10	10	10	40
Casodex - Emerging ROW	31	28	31	23	113	31	34	34	25	125	35	35	35	30	135	40	40	35	30	145
Casodex - Worldwide	52	52	51	46	201	48	57	52	45	200	50	55	45	45	195	55	50	45	40	190
Zoladex - U.S.	$1	$2	$3	$2	$8	$2	$2	$1	$0	$5	$5	$0	$0	$0	$5	$5	$0	$0	$0	$5
Zoladex - E.U. (lc, ex fx)									30		30	30	30	30		30	30	25	25	
Zoladex - E.U.	34	34	31	34	133	35	30	35	30	130	30	30	30	30	120	30	30	25	25	110
Zoladex - Estab. ROW	48	55	49	50	202	43	44	46	45	180	40	40	40	40	160	35	35	35	35	140
Zoladex - Emerging ROW	101	101	111	96	409	114	121	145	105	485	125	130	155	115	525	135	140	165	125	565
Zoladex - Worldwide	184	192	194	182	752	194	197	227	180	800	200	200	225	185	810	205	205	225	185	820
Iressa - U.S.	$8	$6	$6	$6	$26	$4	$4	$6	$5	$20	$5	$5	$5	$0	$15	$5	$5	$0	$0	$10
Iressa - E.U. (lc, ex fx)									15		20	15	10	10		15	10	10	10	
Iressa - E.U.	30	31	24	24	109	26	20	15	15	75	20	15	10	10	55	15	10	10	10	45
Iressa - Estab. ROW	23	29	23	22	97	18	16	8	5	45	5	5	5	5	20	5	5	5	0	15
Iressa - Emerging ROW	71	77	78	60	286	86	78	63	50	275	75	70	55	45	245	70	65	50	40	225
Iressa - Worldwide	132	143	131	112	518	134	118	92	75	420	105	95	75	60	335	95	85	65	50	295
Faslodex - U.S.	$134	$125	$135	$143	$537	$126	$125	$60	$55	$365	$50	$45	$40	$35	$170	$30	$25	$20	$15	$90
Faslodex - E.U. (lc, ex fx)									45		50	50	50	40		45	45	45	35	
Faslodex - E.U.	59	59	53	50	221	54	56	58	45	215	50	50	50	40	190	45	45	45	35	170
Faslodex - Estab. ROW	22	31	30	33	116	29	35	38	35	135	30	40	40	40	150	35	40	45	45	165
Faslodex - Emerging ROW	39	32	40	43	154	45	51	49	45	190	50	55	55	50	210	55	60	60	55	230
Faslodex - Worldwide	254	247	258	269	1,028	254	267	205	180	905	180	190	185	165	720	165	170	170	150	655
Lynparza - U.S.	$66	$83	$84	$112	$345	$119	$143	$170	$190	$620	$210	$230	$250	$270	$960	$290	$310	$330	$350	$1,280
Lynparza - E.U. (lc, ex fx)									80		80	85	90	95		95	100	105	110	
Lynparza - E.U.	42	45	50	53	190	65	66	77	80	290	80	85	90	95	350	95	100	105	110	410
Lynparza - Estab. ROW	3	12	20	26	61	27	41	38	40	145	45	50	55	60	210	65	70	75	80	290
Lynparza - Emerging ROW	8	10	15	18	51	26	33	42	45	145	40	45	50	55	190	55	60	65	70	250
Lynparza - Worldwide	119	150	169	209	647	237	283	327	355	1,200	375	410	445	480	1,710	505	540	575	610	2,230

Source: Company data, Cowen and Company estimates

AstraZeneca Quarterly Product Line Buildup ($MM) (continued)

	Q1:18	Q2:18	Q3:18	Q4:18	2018	Q1:19	Q2:19	Q3:19	Q4:19E	2019E	Q1:20E	Q2:20E	Q3:20E	Q4:20E	2020E	Q1:21E	Q2:21E	Q3:21E	Q4:21E	2021E
Tagrisso - U.S.	$147	$194	$239	$289	$869	$259	$300	$350	$375	$1,285	$400	$425	$450	$475	$1,750	$485	$510	$540	$565	$2,100
Tagrisso - E.U. (lc, ex fx)									135		145	155	165	175		170	180	195	205	
Tagrisso - E.U.	69	70	83	92	314	100	112	125	135	470	145	155	165	175	640	170	180	195	205	750
Tagrisso - Estab. ROW	51	70	77	132	330	133	181	192	180	685	200	220	240	260	920	285	305	325	345	1,260
Tagrisso - Emerging ROW	71	88	107	81	347	138	191	224	250	805	270	290	310	330	1,200	345	365	385	405	1,500
Tagrisso - Worldwide	338	422	506	594	1,860	630	784	891	940	3,245	1,015	1,090	1,165	1,240	4,510	1,285	1,360	1,445	1,520	5,610
Others - U.S.	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Others - E.U. (lc, ex fx)									5		0	5	5	5		5	5	5	5	
Others - E.U.	1	2	0	3	6	1	2	2	5	10	0	5	5	5	15	5	5	5	5	20
Others - Estab. ROW	19	26	18	14	77	11	18	13	20	60	10	20	15	25	70	15	20	20	25	80
Others - Emerging ROW	7	9	10	6	32	8	8	7	10	35	10	10	10	10	40	10	10	10	15	45
Others - Worldwide	27	37	28	23	115	20	28	22	35	105	20	35	30	40	125	30	35	35	45	145
Imfinzi - U.S.	$62	$116	$170	$216	$564	$231	$242	$286	$320	$1,080	$350	$375	$400	$430	$1,555	$470	$500	$525	$555	$2,050
Imfinzi - E.U. (lc, ex fx)									60		60	65	70	80		85	95	100	110	
Imfinzi - E.U.	0	3	6	18	27	23	37	55	60	175	60	65	70	80	275	85	95	100	110	390
Imfinzi - Estab. ROW	0	0	10	26	36	35	53	65	75	230	75	80	85	90	330	105	110	115	120	450
Imfinzi - Emerging ROW	0	3	1	2	6	6	6	6	5	25	10	10	10	10	40	15	15	15	15	60
Imfinzi - Worldwide	62	122	187	262	633	295	338	412	460	1,505	495	530	565	610	2,200	675	720	755	800	2,950
Calquence	8	12	18	24	62	29	35	44	55	165	65	75	85	95	320	110	120	130	140	500
Tremelimumab													5	10	15	20	30	45	55	150
Selumetinib													5	10	15	15	20	25	30	90
Savolitinib/Volitinib																		20	30	50
Capivasertib																				
Monalizumab																				
Adavosertib																				
Ceralasertib																				
AZD2811																				
Oleclumab																				
Danvatirsen																				
AZD4635																				
Trastuzumab Collaboration													15	35	65	40	50	60	65	215
Oncology	**$1,230**	**$1,434**	**$1,597**	**$1,767**	**$6,028**	**$1,892**	**$2,167**	**$2,334**	**$2,370**	**$8,765**	**$2,560**	**$2,735**	**$2,905**	**$3,030**	**$11,245**	**$3,255**	**$3,445**	**$3,650**	**$3,775**	**$14,125**
% Change	39%	44%	56%	58%	50%	54%	51%	46%	34%	45%	35%	26%	24%	28%	28%	27%	26%	26%	25%	26%

Source: Company data, Cowen and Company estimates

AstraZeneca Quarterly Product Line Buildup ($MM) (continued)

	Q1:18	Q2:18	Q3:18	Q4:18	2018	Q1:19	Q2:19	Q3:19	Q4:19E	2019E	Q1:20E	Q2:20E	Q3:20E	Q4:20E	2020E	Q1:21E	Q2:21E	Q3:21E	Q4:21E	2021E
Neuroscience	**$122**	**$153**	**$0**	**$0**	**$275**	**$37**	**$32**	**$82**	**$0**	**$150**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
% Change	-42%	15%	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Synagis - U.S.	$134	$9	$8	$154	$287	$25	$10	$1		$36										
Synagis - E.U. (lc, ex fx)									90		40	25	135	80		35	20	130	75	
Synagis - E.U.	90	35	156	96	377	28	86	144	90	350	40	25	135	80	280	35	20	130	75	260
Synagis - Estab. ROW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Synagis - Emerging ROW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Synagis - Worldwide	224	26	164	251	665	53	96	145	90	385	40	25	135	80	280	35	20	130	75	260
FluMist/Fluenz - U.S.	$0	$0	$15	$0	$15	$0	$0	$0	$25	$25	$0	$0	$35	$35	$70	$0	$0	$45	$45	$90
FluMist/Fluenz - E.U. (lc, ex fx)									75		0	0	20	80		0	0	30	80	
FluMist/Fluenz - E.U.	0	0	20	71	91	0	0	0	75	75	0	0	20	80	100	0	0	30	80	110
FluMist/Fluenz - Estab. ROW	0	0	0	3	3	0	0	0	5	5	0	0	0	10	10	0	0	5	10	15
FluMist/Fluenz - Emerging ROW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FluMist/Fluenz - Worldwide	0	0	35	75	110	0	0	0	105	105	0	0	55	125	180	0	0	80	135	215
Others - U.S.	$5	$0	$5	$15	$25	$3	$8	$18	$20	$50	$5	$5	$15	$30	$55	$5	$10	$15	$30	$60
Others - E.U. (lc, ex fx)									25		10	10	5	35		10	15	10	35	
Others - E.U.	0	0	5	30	35	8	13	18	25	65	10	10	5	35	60	10	15	10	35	70
Others - Estab. ROW	5	0	5	7	17	7	-7	0	10	10	5	5	0	5	15	5	5	0	10	20
Others - Emerging ROW	8	0	83	25	116	-1	16	-5	20	30	5	5	5	20	35	5	5	5	25	40
Others - Worldwide	18	0	98	77	193	17	30	31	75	155	25	25	25	90	165	25	35	30	100	190
Roxadustat									15	15	20	40	80	100	240	110	130	170	190	600
Verinurad																				
MEDI7352																				
MEDI3902																				
Suvratoxumab																				
Nirsevimab																				
Anifrolumab																				
Vimovo	20	17	15	15	67															
Zinforo																				
Other	**$262**	**$43**	**$312**	**$418**	**$1,035**	**$70**	**$126**	**$176**	**$285**	**$660**	**$85**	**$90**	**$295**	**$395**	**$865**	**$170**	**$185**	**$410**	**$500**	**$1,265**
% Change	5%	-82%	42%	19%	-3%	-73%	193%	-44%	-32%	-36%	21%	-29%	68%	39%	31%	100%	106%	39%	27%	46%
TOTAL PHARMA	**$4,985**	**$5,030**	**$5,266**	**$5,768**	**$21,049**	**$5,465**	**$5,718**	**$6,132**	**$6,275**	**$23,600**	**$6,135**	**$6,235**	**$6,795**	**$7,045**	**$26,225**	**$7,000**	**$7,130**	**$7,700**	**$8,010**	**$29,840**
% Change	3%	2%	8%	5%	4%	10%	14%	16%	9%	12%	12%	9%	11%	12%	11%	14%	14%	13%	14%	14%
COLLABORATION REVENUE																				
Co-development, commercialization, partnerships	$193	$125	$74	$649	$1,041	$26	$105	$274	$400	$805	$100	$150	$165	$150	$565	$80	$130	$145	$130	$485
AZN Territory Profit from Diiachi Collaboration											20	20	15	0	-54	10	15	20	25	70
Total Collaboration Revenue	$193	$125	$74	$649	$1,041	$26	$105	$274	$400	$805	$80	$130	$150	$150	$510	$90	$145	$165	$155	$555
% Change	-66%	13%	-95%	124%	-55%	-87%	-16%	270%	-38%	-23%	208%	24%	-45%	-63%	-37%	13%	12%	10%	3%	9%
TOTAL AZN	**$5,178**	**$5,155**	**$5,340**	**$6,417**	**$22,090**	**$5,491**	**$5,823**	**$6,406**	**$6,675**	**$24,405**	**$6,215**	**$6,365**	**$6,945**	**$7,195**	**$26,735**	**$7,090**	**$7,275**	**$7,865**	**$8,165**	**$30,395**
% Change	-4%	2%	-14%	11%	-2%	6%	13%	20%	4%	10%	13%	9%	8%	8%	10%	14%	14%	13%	13%	14%

Source: Company data, Cowen and Company estimates

AstraZeneca Annual Product Line Buildup ($MM)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comment
Nexium - U.S.	$306	$225	$150	$70	$50	$30	$10	$5	-30%	-44%	Generics launched 2/15
Nexium - E.U. (lc, ex fx)											
Nexium - E.U.	235	50									Rights to Nexium EU and Vimovo sold to Grunenthal for $700MM upfront and up to $90MM in sales-related payments; completed in 2018
Nexium - Estab. ROW	471	420	380	340	300	250	200	150	-10%	-15%	Patent expires 7/20/20 in Japan; Japan, Canada, Australia, New Zealand
Nexium - Emerging ROW	690	750	770	790	810	830	850	870	6%	3%	No generics in China yet
Nexium - Worldwide	1,702	1,445	1,300	1,200	1,160	1,110	1,060	1,025	-13%	-7%	Generics/OTC products pressure market
Losec - U.S.	$7	$5	$5	$5	$5	$5	$5	$5	-15%	-5%	
Losec - E.U. (lc, ex fx)											
Losec - E.U.	70	50	0	0	0	0	0	0	NM	NM	EU rights sold to Cheplopharm
Losec - Estab. ROW	34	25	15	10	5	5	5	5	-34%	-24%	Japan, Canada, Australia, New Zealand
Losec - Emerging ROW	161	180	200	220	240	260	280	300	11%	9%	
Losec - Worldwide	272	260	220	235	250	270	290	310	-10%	2%	Off patent in many markets
Movantik/Moventig	109	95	90	85	80	75	70	65	-9%	-7%	Naloxegol; oral peripherally-acting opioid antag.; opioid-induced constipation; co-commercialization with Daiichi in U.S.; launched in Nordic countries, EU and Canada
Axanum	3	0	0	0	0	0	0	0	NM	NM	Nexium/low-dose aspirin combo; generics pressure EU, Japan; U.S. filing withdrawn
Gastrointestinal	**$2,080**	**$1,800**	**$1,610**	**$1,520**	**$1,490**	**$1,455**	**$1,420**	**$1,400**	**-12%**	**-5%**	
% Change	-11%	-13%	-11%	-6%	-2%	-2%	-2%	-1%			
Crestor - U.S.	$170	$120	$80	$60	$40	$20	$10	$5	-31%	-40%	Patent expired July 2016 (included pedi exclusivity); numerous generics launched
Crestor - E.U. (lc, ex fx)											
Crestor - E.U.	203	145	115	85	65	45	25	15	-25%	-31%	Patent expired June 2017
Crestor - Estab. ROW	219	210	175	135	100	75	50	25	-11%	-27%	LOE in Canada pressures; Japan, Canada, Australia, New Zealand
Crestor - Emerging ROW	841	840	800	760	720	680	640	600	-2%	-5%	Did not compete for access in China
Crestor - Worldwide	1,433	1,320	1,170	1,040	925	820	725	645	-10%	-11%	
Seloken/Toprol XL - U.S.	$39	$35	$30	$25	$20	$15	$10	$5	NM	NM	Outlicensed 10/16
Seloken/Toprol XL - E.U. (lc, ex fx)											
Seloken/Toprol XL - E.U.	19	20	15	10	5	5	5	5	-11%	-17%	
Seloken/Toprol XL - Estab. ROW	13	10	5	5	5	5	5	5	NM	NM	Japan, Canada, Australia, New Zealand
Seloken/Toprol XL - Emerging ROW	641	670	710	750	790	830	870	910	5%	5%	
Seloken/Toprol XL - Worldwide	712	730	760	790	820	855	890	925	3%	4%	AZN brand, Par authorized generic, and Watson on market; Sandoz a threat
Atacand - U.S.	$13	$10	$5	$5	$5	$5	$5	$5	-38%	-13%	U.S. patent expired 6/12
Atacand - E.U. (lc, ex fx)											
Atacand - E.U.	70	20									EU rights licensed to Cheplapharm Q3:18
Atacand - Estab. ROW	20	15	10	5	5	5	5	5	-29%	-18%	Japan, Canada, Australia, New Zealand
Atacand - Emerging ROW	157	155	130	110	90	70	50	30	-9%	-21%	
Atacand - Worldwide	260	200	145	120	100	80	60	40	-25%	-23%	A2 antagonist

Source: Company data, Cowen and Company estimates

AstraZeneca Annual Product Line Buildup ($MM) (continued)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comment
Onglyza - U.S.	$223	$225	$195	$175	$155	$135	$115	$95	-6%	-11%	3.3% market share in U.S. 11/19; no AZN sales support; Komboglyze (Onglyza/metformin combo) launched as QD
Onglyza - E.U. (lc, ex fx)											
Onglyza - E.U.	89	70	60	50	40	30	20	10	-18%	-27%	Komboglyze (Onglyza/metformin combination) launched as BID
Onglyza - Estab. ROW	59	55	50	45	40	35	30	25	-8%	-12%	Japan, Canada, Australia, New Zealand
Onglyza - Emerging ROW	172	185	170	150	130	110	90	70	-1%	-12%	
Onglyza - Worldwide	543	530	475	420	365	310	255	200	-6%	-13%	Saxagliptin; DPP-IV inhib; SAVOR-TIMI 54 showed no CV benefit, hint of risk; SGLT2s a headwind
Brilinta - U.S.	$588	$695	$780	$860	$960	$1,040	$900	$700	15%	3%	7.9% market share in U.S. 11/19; patent term extension should run to 10/24 but other patents may protect; 1+ year tx approved 9/15
Brilinta - E.U. (lc, ex fx)											
Brilinta - E.U.	348	355	390	430	470	510	550	500	6%	5%	SPC should retain exclusivity to 12/24
Brilinta - Estab. ROW	59	60	65	70	75	80	85	90	5%	6%	Japan, Canada, Australia, New Zealand
Brilinta - Emerging ROW	326	480	440	400	350	300	250	200	16%	-7%	Patent expiration in 2019
Brilinta - Worldwide	1,321	1,590	1,675	1,760	1,855	1,930	1,785	1,490	13%	2%	Reversible ADP rec. antag; oral; arterial thrombosis; ACS apprd; $2B potential, down from $4B, given trial failures
Bydureon - U.S.	$475	$450	$445	$465	$485	$505	$525	$545	-3%	2%	Once-weekly GLP1; BCise dual chamber pen device launched; 7.5% share 11/19
Bydureon - E.U. (lc, ex fx)											
Bydureon - E.U.	81	70	75	80	85	90	95	100	-4%	3%	Autoinjector H2:18
Bydureon - Estab. ROW	20	15	20	25	30	35	40	45	0%	12%	Japan, Canada, Australia, New Zealand
Bydureon - Emerging ROW	8	10	15	20	25	30	35	40	37%	26%	
Bydureon - Worldwide	584	545	555	590	625	660	695	730	-3%	3%	Synthetic exendin-4; BMY's 50% stake acquired Q1:14
Byetta - U.S.	$74	$65	$55	$45	$35	$25	$15	$5	-14%	-32%	Twice daily GLP1; patent litigation settlement allowed Teva to launch generic on 10/15/17
Byetta - E.U. (lc, ex fx)											
Byetta - E.U.	29	20	15	10	5	5	5	5	-28%	-22%	Generics launched but impact limited thus far
Byetta - Estab. ROW	15	15	10	5	5	5	5	5	-18%	-15%	Japan, Canada, Australia, New Zealand
Byetta - Emerging ROW	8	10	10	10	10	10	10	10	12%	3%	
Byetta - Worldwide	126	110	90	70	55	45	35	25	-15%	-21%	Synthetic exendin-4; BMY's 50% stake acquired Q1:14
Farxiga - U.S.	$591	$545	$575	$605	$635	$665	$695	$725	-1%	3%	Qtern (saxa/dapa) approved 2/17, launched 2018; T1DM CRL received
Forxiga - E.U. (lc, ex fx)											
Forxiga - E.U.	315	370	410	450	500	550	600	650	14%	11%	Saxa/Dapa launched in 2016; T1DM approved
Forxiga - Estab. ROW	149	165	180	200	225	250	275	300	10%	11%	T1DM H1:19 approved
Forxiga - Emerging ROW	336	475	535	585	625	665	700	735	26%	12%	On China NRDL YE 2019
Farxiga - Worldwide	1,391	1,555	1,700	1,840	1,985	2,130	2,270	2,410	11%	8%	Dapagliflozin; SGLT2 inhibitor;diabetes; DECLARE CV study hit 1 of 2 endpoints
Others - U.S.	$5	$5	$0	$0	$0	$0	$0	$0	NM	NM	
Others - E.U. (lc, ex fx)											
Others - E.U.	61	70	60	50	40	30	20	10	-1%	NM	
Others - Estab. ROW	27	20	15	10	5	5	5	5	-25%	-21%	Japan, Canada, Australia, New Zealand
Others - Emerging ROW	233	180	160	140	120	100	80	60	-17%	-18%	
Others - Worldwide	326	275	235	200	165	135	105	75	-15%	-19%	

Source: Company data, Cowen and Company estimates

AstraZeneca Annual Product Line Buildup ($MM) (continued)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comment
Lokelma		20	30	50	100	150	200	250	NM	NM	Hyperkalemia in CKD/CHF; zirconium silicate (ZS-9), not absorbed; approved U.S. 5/18; EU 3/18; launch 2019; Japan filing 2019; pat. exp 2032; via ZS Pharma
Epanova				50	100	150	200	250	NM	NM	Hypertriglyceridemia; omega-3 free fatty acid composition; apprvd U.S.; Japan filing '20; Omthera acquired 7/8/13; launch awaits STRENGTH outcomes data
Cotadutide							25	50	NM	NM	GLP-1/glucagon co-agonist; Phase II diabetes/obesity; PII in NASH to start H2:19
MEDI5884							25	50	NM	NM	Cholesterol modulation; Phase II
MEDI6012							25	50	NM	NM	ACS; LCAT; Phase II
AZN5718							25	50	NM	NM	FLAP inhibitor; coronary artery disease; Phase IIa, Phase IIb starts H2:19
AZN8601							25	50	NM	NM	VEGF-A mRNA; heart failure; Phase II
AZN4831							25	50	NM	NM	MPO inhibitor; heart failure (HFpEF); Phase II
Symlin	34	35	40	45	50	55	60	65	8%	10%	Pramlintide
Cardiovascular	**$6,730**	**$6,910**	**$6,875**	**$6,975**	**$7,145**	**$7,320**	**$7,430**	**$7,405**	**1%**	**1%**	
% Change	-7%	3%	-1%	1%	2%	2%	2%	0%			
Fasenra - U.S.	$218	$490	$680	$840	$1,000	$1,100	$1,200	$1,300	77%	29%	Self-injector regulatory decision H2:19
Fasenra - E.U. (lc, ex fx)											
Fasenra - E.U.	32	120	170	250	300	350	400	450	130%	46%	Self-injector regulatory decision H2:19
Fasenra - Estab. ROW	46	105	190	260	325	400	475	550	103%	43%	Approved Japan
Fasenra - Emerging ROW	1	10	20	40	60	80	100	120	NM	NM	
Fasenra - Worldwide	297	725	1,060	1,390	1,685	1,930	2,175	2,420	89%	35%	Benralizumab; IL-5R mAb; severe asthma: COPD trials failed
Symbicort - U.S.	$862	$775	$650	$550	$450	$350	$250	$150	-13%	-22%	4.1% market share in U.S. 11/19; stable volume but price pressure
Symbicort - E.U. (lc, ex fx)											
Symbicort - E.U.	773	670	575	475	375	275	175	75	-14%	-28%	Teva generic filing 2013; Adavir generics pressure
Symbicort - Estab. ROW	431	410	375	335	295	250	200	150	-7%	-14%	Japan, Canada, Australia, New Zealand
Symbicort - Emerging ROW	495	540	585	625	665	705	745	785	9%	7%	
Symbicort - Worldwide	2,561	2,395	2,185	1,985	1,785	1,580	1,370	1,160	-8%	-11%	
Pulmicort - U.S.	$116	$120	$105	$85	$65	$45	$25	$5	-5%	-36%	Respules for nebulizer (infants) patent ruled invalid, generics launched
Pulmicort - E.U. (lc, ex fx)											
Pulmicort - E.U.	90	80	70	60	50	40	30	20	-12%	-19%	
Pulmicort - Estab. ROW	85	80	75	70	65	60	55	50	-6%	-7%	Japan, Canada, Australia, New Zealand
Pulmicort - Emerging ROW	995	1,170	1,250	1,330	1,400	1,475	1,550	1,625	12%	7%	More than 50% from China
Pulmicort - Worldwide	1,286	1,450	1,500	1,545	1,580	1,620	1,660	1,700	8%	4%	
Tudorza/Eklira - U.S.	$25	$5	$5	$5	$5	$5	$5	$5	-55%	-21%	Co-promote with Circassia in U.S. (3/17)
Tudorza/Eklira - E.U. (lc, ex fx)											
Tudorza/Eklira - E.U.	74	65	75	85	95	105	115	125	1%	8%	
Tudorza/Eklira - Estab. ROW	10	10	15	20	25	30	35	40	22%	22%	
Tudorza/Eklira - Emerging ROW	1	5	10	15	20	25	30	35	216%	66%	
Tudorza/Eklira - Worldwide	110	85	105	125	145	165	185	205	-2%	9%	Aclidinium (LAMA); via Almirall resp acq for $875MM and $1.22B in milestones
Daliresp/Daxas - U.S.	$155	$180	$195	$210	$225	$240	$255	$270	12%	8%	US rights acquired from Actavis Q1:15
Daliresp/Daxas - E.U. (lc, ex fx)											
Daliresp/Daxas - E.U.	28	30	35	40	45	50	55	60	12%	12%	OUS rights acquired Q1:16
Daliresp/Daxas - Estab. ROW	1	0	0	0	0	0	0	0	NM	NM	
Daliresp/Daxas - Emerging ROW	5	5	5	5	5	5	5	5	NM	NM	
Daliresp/Daxas - Worldwide	189	210	235	255	275	295	315	335	12%	9%	Roflumilast; PDE4 inhibitor; COPD; via Actavis in 3/15
Duaklir - U.S.	$0	$0	$0	$0	$0	$0	$0	$0	NM	NM	Circassia U.S. rights with royalties to AZN; COPD approved 3/19
Duaklir - E.U. (lc, ex fx)											
Duaklir - E.U.	91	75	75	80	85	90	95	100	-9%	1%	
Duaklir - Estab. ROW	3	5	10	15	20	25	30	35	83%	42%	
Duaklir - Emerging ROW	1	0	0	0	0	0	0	0	NM	NM	
Duaklir - Worldwide	95	80	85	95	105	115	125	135	-5%	5%	Aclidinium/formoterol; BID inhalation; COPD
Others - U.S.	$2	$0	$0	$0	$0	$0	$0	$0	NM	NM	
Others - E.U. (lc, ex fx)											
Others - E.U.	144	85	80	75	70	65	60	55	-25%	-13%	
Others - Estab. ROW	48	10	15	20	25	30	35	40	-44%	-3%	Japan, Canada, Australia, New Zealand
Others - Emerging ROW	140	225	240	255	270	285	300	315	31%	12%	
Others - Worldwide	330	320	335	350	365	380	395	410	1%	3%	Accolate, Oxis (OUS)

Source: Company data, Cowen and Company estimates

AstraZeneca Annual Product Line Buildup ($MM) (continued)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comment
Bevespi Aerosphere	33	45	75	110	175	225	275	325	51%	39%	PT003; LABA/LAMA, formoterol/glycopyrrolate; COPD; marketed U.S., EU, JP
Breztri (PT010)		5	50	100	150	200	250	300	NM	NM	LABA/LAMA/ICS, COPD; JP approved 2019; U.S./EU filings H2:19; asthma Phase II
PT027					50	100	150	150	NM	NM	SABA/ICS; asthma; Phase III initiated H1:19
Tezepelumab					50	100	150	150	NM	NM	TSLP mAb; severe asthma PIII; filing 2021 US, EU, JP; PII atopic dermatitis/COPD
AZN8871							25	50	NM	NM	MABA; COPD; Phase II
Abediterol							25	50	NM	NM	QD LABA; asthma/COPD; Phase II; via Almirall
AZN7594							25	50	NM	NM	Inhaled SGRM modulator; asthma/COPD; Phase II
AZN9567							25	50	NM	NM	Oral SGRM; RA/respiratory; Phase II
AZN1402							25	50	NM	NM	IL-4R antagonist; asthma; Phase II start H2:19
AZN7986							25	50	NM	NM	DPP1; COPD; Phase II
Respiratory	**$4,901**	**$5,315**	**$5,630**	**$5,955**	**$6,365**	**$6,710**	**$7,200**	**$7,590**	**7%**	**6%**	
% Change	4%	8%	6%	6%	7%	5%	7%	5%			
Arimidex - U.S.	$0	$0	$5	$5	$5	$5	$5	$5	NM	NM	Generics launched 6/10
Arimidex - E.U. (lc, ex fx)											
Arimidex - E.U.	31	25	20	15	10	5	5	5	-20%	-23%	Patent expired 8/10 but exclusivity extended until 2/11
Arimidex - Estab. ROW	49	45	40	35	30	25	20	15	-10%	-16%	Japan, Canada, Australia, New Zealand
Arimidex - Emerging ROW	132	150	160	170	180	190	200	210	10%	7%	
Arimidex - Worldwide	212	220	225	225	225	225	230	235	3%	1%	Aromatase inhibitor (AI); breast cancer
Casodex - U.S.	$1	$0	$0	$0	$0	$0	$0	$0	NM	NM	Patent expired 10/08
Casodex - E.U. (lc, ex fx)											
Casodex - E.U.	20	15	10	5	5	5	5	5	-29%	-18%	
Casodex - Estab. ROW	67	60	50	40	30	20	10	5	-14%	-31%	Japan, Canada, Australia, New Zealand
Casodex - Emerging ROW	113	125	135	145	155	165	175	185	9%	7%	
Casodex - Worldwide	201	200	195	190	190	190	190	195	-2%	0%	Non-steroidal anti-androgen; prostate cancer
Zoladex - U.S.	$8	$5	$5	$5	$5	$5	$5	$5	-21%	-6%	
Zoladex - E.U. (lc, ex fx)											
Zoladex - E.U.	133	130	120	110	100	90	80	70	-5%	-9%	
Zoladex - Estab. ROW	202	180	160	140	120	100	80	60	-11%	-16%	Japan, Canada, Australia, New Zealand
Zoladex - Emerging ROW	409	485	525	565	605	645	685	725	13%	9%	
Zoladex - Worldwide	752	800	810	820	830	840	850	860	4%	2%	LHRH agonist; prostate cancer, gyn/fertility disorders; 70% of use is 3 month release where no generics; no generics for one month depot
Iressa - U.S.	$26	$20	$15	$10	$5	$5	$5	$5	-24%	-21%	Patent expiration 2022, but focus on Tagrisso
Iressa - E.U. (lc, ex fx)											
Iressa - E.U.	109	75	55	45	35	25	15	5	-29%	-36%	Patent expiration 2019, but focus on Tagrisso
Iressa - Estab. ROW	97	45	20	15	10	5	5	5	-55%	-35%	Japan, Canada, Australia, New Zealand
Iressa - Emerging ROW	286	275	245	225	200	175	150	125	-7%	-11%	China drives growth
Iressa - Worldwide	518	420	335	295	250	210	175	140	-20%	-17%	EGFR positive NSCLC
Faslodex - U.S.	$537	$365	$170	$90	$75	$50	$25	$5	-44%	-49%	Substance pat exp. 2019; via settlement, Sandoz generic launched 3/25/19
Faslodex - E.U. (lc, ex fx)											
Faslodex - E.U.	221	215	190	170	150	130	110	90	-7%	-12%	Generics launched Germany and Spain; at risk in some other markets
Faslodex - Estab. ROW	116	135	150	165	180	195	210	225	14%	10%	Japan, Canada, Australia, New Zealand; Japan patent expires 2026
Faslodex - Emerging ROW	154	190	210	230	250	270	290	310	17%	11%	
Faslodex - Worldwide	1,028	905	720	655	655	645	635	630	-16%	-7%	EGFR positive NSCLC; new 1st line breast claim/combo with CDK4/6 inhibitors
Lynparza - U.S.	$345	$620	$960	$1,280	$1,500	$1,700	$1,900	$2,100	67%	29%	1L, 2L ovarian cancer and 2L BC approved; to be filed in pancreatic, BRCA mCRPC
Lynparza - E.U. (lc, ex fx)											
Lynparza - E.U.	190	290	350	410	475	550	625	700	36%	20%	Ovarian 2L and 1L, breast cancer approved
Lynparza - Estab. ROW	61	145	210	290	400	500	600	700	86%	42%	Launched in 15 countries
Lynparza - Emerging ROW	51	145	190	250	325	400	475	550	93%	40%	Ovarian 1L approval in China H2:19 and on NRDL as of YE 2019
Lynparza - Worldwide	647	1,200	1,710	2,230	2,700	3,150	3,600	4,050	63%	30%	Olaparib; oral PARP-BRCA; ovarian, breast, gastric, prostate, pancreatic; collaboration with MRK

Source: Company data, Cowen and Company estimates

AstraZeneca Annual Product Line Buildup ($MM) (continued)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comment
Tagrisso - U.S.	$869	$1,285	$1,750	$2,100	$2,350	$2,600	$2,850	$3,100	42%	20%	Launched U.S.
Tagrisso - E.U. (lc, ex fx)											
Tagrisso - E.U.	314	470	640	750	850	950	1,050	1,150	43%	20%	Launched EU
Tagrisso - Estab. ROW	330	685	920	1,260	1,500	1,700	1,900	2,100	67%	30%	Launched Japan, 1L in H2:18; price cut 11/19
Tagrisso - Emerging ROW	347	805	1,200	1,500	1,700	1,900	2,100	2,300	86%	31%	1L regulatory decision in China H2:19
Tagrisso - Worldwide	1,860	3,245	4,510	5,610	6,400	7,150	7,900	8,650	56%	25%	EGFRm+; T790M+ NSCLC 1st line; solid tumors in Phase I; $4B potential in G7 countries
Others - U.S.	$0	$0	$0	$0	$0	$0	$0	$0	NM	NM	
Others - E.U. (lc, ex fx)											
Others - E.U.	6	10	15	20	25	30	35	40	58%	31%	
Others - Estab. ROW	77	60	70	80	100	120	140	160	-5%	11%	Japan, Canada, Australia, New Zealand
Others - Emerging ROW	32	35	40	45	50	55	60	65	12%	11%	
Others - Worldwide	115	105	125	145	175	205	235	265	4%	13%	Faslodex, Nolvadex, Tomudex
Imfinzi - U.S.	$564	$1,080	$1,555	$2,050	$2,300	$2,450	$2,720	$3,000	66%	27%	U.S. approved 2L bladder, unresectable Stage III NSCLC
Imfinzi - E.U. (lc, ex fx)											
Imfinzi - E.U.	27	175	275	390	555	650	725	800	219%	62%	Unresectable Stage III NSCLC H2:18
Imfinzi - Estab. ROW	36	230	330	450	600	675	725	775	203%	55%	
Imfinzi - Emerging ROW	6	25	40	60	80	110	140	170	158%	61%	Unresectable Stage III NSCLC in China H2:19
Imfinzi - Worldwide	633	1,505	2,200	2,950	3,535	3,885	4,310	4,745	86%	33%	Durvalumab; PD-L1; Ph III in SCCHN, lung and H&N w/treme, other solid tumors
Calquence	62	165	320	500	700	900	1,100	1,300	127%	54%	Acalabutinib; BTKi; apprd: MCL; trials: CLL/SLL, DLBCL, FL, MM, WM, NHL; via 55% stake in Acerta
Tremelimumab			15	150	200	250	300	350	NM	NM	Anti-CTLA4 Mab; lung cancer, combo with PD-L1; Phase III
Selumetinib			15	90	150	200	250	300	NM	NM	MEK inhib. shorter t1/2; neurofibromatosis type-1 filings H2:19, 2L NSCLC Phase II
Savolitinib/Volitinib				50	100	150	200	200	NM	NM	MET inhibitor; papillary renal cell carcinoma; Phase III; U.S., EU NDA 2020
Capivasertib					50	100	150	150	NM	NM	AZD5363; AKT inhibitor; breast, prostate cancer; Phase III initiated Q3:19
Monalizumab							25	50	NM	NM	NKG2a mAb; head & neck, colorectal; Phase II
Adavosertib									NM	NM	AZN1775; Wee1 kinase inhib; oral small molecule; combos in ovarian (PII), solid tumors (PII initiated H1:19)
							25	50			
Ceralasertib							25	50	NM	NM	ATR inhibitor; combo with Lynparza; solid tumors, Phase II initiated H1:19
AZD2811							25	50	NM	NM	Aurora B inhib.; SCLC, solid tumors/blood cancers; Phase I/II
Oleclumab							25	50	NM	NM	CD73 mAb; lung, pancreatic cancers; Phase II
Danvatirsen							25	50	NM	NM	STAT3 inhibitor; bladder, H&N, lung; Phase I/II
AZD4635							25	50	NM	NM	A2AR inhibitor; solid tumor, Phase II
Trastuzumab Collaboration			65	215	335	415	500	585	NM	NM	With Daiichi Sankyo; launched 1/20 for refractory BC; $1.35B upfront split btw 2019/20; regulatory/other payments totaling up to $3.8B, milestones up to $1.75B; royalties
Oncology	**$6,028**	**$8,765**	**$11,245**	**$14,125**	**$16,495**	**$18,515**	**$20,800**	**$23,005**	**37%**	**21%**	
% Change	50%	45%	28%	26%	17%	12%	12%	11%			

Source: Company data, Cowen and Company estimates

AstraZeneca Annual Product Line Buildup ($MM) (continued)

	2018	2019E	2020E	2021E	2022P	2023P	2024P	2025P	2018-20 CGR	2018-25 CGR	Comment
Neuroscience	**$275**	**$150**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**NM**	**NM**	Seroquel XR/IR in EU/Russia sold to Cheplapharm for $178MM upfront in 10/19
% Change	NM	NM	NM	NM	NM	NM	NM	NM			
Synagis - U.S.	$287	$36							NM	NM	Sold to Sobi for $1B cash and $500MM in Sobi shares; closed Jan 2019
Synagis - E.U. (lc, ex fx)											
Synagis - E.U.	377	350	280	260	240	220	200	180	-14%	-10%	
Synagis - Estab. ROW	0	0	0	0	0	0	0	0	NM	NM	Japan, Canada, Australia, New Zealand
Synagis - Emerging ROW	1	0	0	0	0	0	0	0	NM	NM	
Synagis - Worldwide	665	385	280	260	240	220	200	180	-35%	-17%	Humanized Mab binds to F-protein of RSV
FluMist/Fluenz - U.S.	$15	$25	$70	$90	$110	$130	$150	$170	116%	41%	CDC recommends use for 2018-19 flu season
FluMist/Fluenz - E.U. (lc, ex fx)											
FluMist/Fluenz - E.U.	91	75	100	110	120	130	140	150	5%	7%	
FluMist/Fluenz - Estab. ROW	3	5	10	15	20	25	30	35	83%	42%	Japan, Canada, Australia, New Zealand
FluMist/Fluenz - Emerging ROW	1	0	0	0	0	0	0	0	NM	NM	
FluMist/Fluenz - Worldwide	110	105	180	215	250	285	320	355	28%	18%	Intranasal influenza vaccine for healthy patients age 2-49 years
Others - U.S.	$25	$50	$55	$60	$65	$70	$75	$80	48%	18%	
Others - E.U. (lc, ex fx)											
Others - E.U.	35	65	60	70	80	90	100	100	31%	16%	
Others - Estab. ROW	17	10	15	20	25	30	35	40	-6%	13%	Japan, Canada, Australia, New Zealand
Others - Emerging ROW	116	30	35	40	45	50	55	60	-45%	-9%	
Others - Worldwide	193	155	165	190	215	240	265	280	-8%	5%	
Roxadustat		15	240	600	800	1,050	1,300	1,550	NM	NM	Hypoxia-induced factor prolyl hydroxylase inhibitor; anemia in CKD/ESRD; NDA US (H2:19), China apprv'd 12/18 and on NRDL YE 2019; AZN books sales in US, FGEN books in China
Verinurad							25	50	NM	NM	RDEA3170; selective uric acid reabsorption inhibitor; CKD; Phase II
MEDI7352							25	50	NM	NM	NGF/TNF; OA, painful diabetic neuropathy; Phase II
MEDI3902							25	50	NM	NM	Psl/PcrV bispecific mAb; prevention of nosocomial pseudomonas pneumonia; Phase II; Q2:16 (fast track)
Suvratoxumab							25	50	NM	NM	mAb binding S. aureus toxin; hospital-acquired pneumonia/serious S. aureus infection; Phase II
Nirsevimab							25	50	NM	NM	RSV mAb-YTE; passive RSV immunization; Phase II (Fast track U.S.); Sobi participates in profits/loses; AZN receives $470MM in sales-related payments + other payments
Anifrolumab					10	20	30	40	NM	NM	MEDI-546; anti-IFN-alphaR MAb; SLE; Phase III trials TULIP-SLE1 missed endpoint, TULIP-SLE2 met endpoint; lupus nephritis Phase II; SC
Vimovo	67										Rights to Vimovo and Nexium EU sold to Grunenthal for $700MM upfront and up to $90MM in sales-related payments; completes in 2018
Zinforo											Sold to PFE along with other small molecule anti-infectives, primarily OUS
Other	**$1,035**	**$660**	**$865**	**$1,265**	**$1,515**	**$1,815**	**$2,240**	**$2,655**	**-9%**	**14%**	
% Change	-3%	-36%	31%	46%	20%	20%	23%	19%			
TOTAL PHARMA	**$21,049**	**$23,600**	**$26,225**	**$29,840**	**$33,010**	**$35,815**	**$39,090**	**$42,055**	**12%**	**10%**	
% Change	4%	12%	11%	14%	11%	8%	9%	8%			
COLLABORATION REVENUE											
Co-development, commercialization, partnerships	$1,041	$805	$565	$485	$400	$350	$300	$250	-26%	-18%	Royalties, milestones; 26% is recurring
AZN Territory Profit from Diiachi Collaboration			-54	70	165	245	325	410			Trastuzumab Deruxtecan
Total Collaboration Revenue	$1,041	$805	$510	$555	$565	$595	$625	$660	-30%	-6%	
% Change	-55%	-23%	-37%	9%	2%	5%	5%	6%			
TOTAL AZN	**$22,090**	**$24,405**	**$26,735**	**$30,395**	**$33,575**	**$36,410**	**$39,715**	**$42,715**	10%	10%	
% Change	-2%	10%	10%	14%	10%	8%	9%	8%			

Source: Company data, Cowen and Company estimates

Oncology

Oncology Portfolio Well Balanced Between Small Molecules And Biologics

AZN has a rich oncology portfolio that includes: targeted therapies (EGFR, MEK, Pi3K, BTK, SERD, KRAS, cMET, MCL1, BRD4), DNA damage repair inhibitors (olaparib, Wee-1, ATR), antibody drug conjugates (moxetumomab, trastuzumab deruxtecan, others) and IO (PD-L1, CTLA-4, OX40, PD-1, others). In IO, Imfinzi is well-positioned in early stage NSCLC with significant room to grow pending important trial readouts over the next few years. Beyond IO, Calquence, Tagrisso, and Lynparza are key growth drivers.

Imfinzi Marketed In Bladder and Unresectable Stage III NSCLC; Metastatic NSCLC Approval Still Possible But Path Is Narrow; 1L SCLC Approval Expected H1:20

Imfinzi (durvalumab/MEDI4736) is an anti-PD-L1 mAb being evaluated across a variety of solid tumors and hematological malignancies as a monotherapy and in combination. Initially, AZN positioned Imfinzi for monotherapy treatment in refractory lines (e.g., 2/3L+ NSCLC, bladder, SCCHN). Current pivotal studies are designed to evaluate Imfinzi +/- tremelimumab (CTLA4 inhibitor) in earlier lines of treatment (i.e. NSCLC, SCLC, HCC, bladder, and gastric cancer). Most recently, AZN has begun evaluating Imfinzi combinations with chemo (i.e. NSCLC, bladder, cervical, TNBC) and other non-chemo therapeutic agents (i.e. NSCLC, HCC, TNBC). We estimate Imfinzi sales of $1.505B (+137%) in 2019, $2.2B in 2020, and $4.745B in 2025.

Durvalumab was first approved for 2L bladder cancer in May 2017. Positive adjuvant data in Stage III unresectable NSCLC (PACIFIC) demonstrated significantly improved PFS (co-primary endpoint; NEJM publication, November 2017), leading to a second FDA approval in February 2018 prior to OS data. AZN announced Imfinzi hit OS in May 2018. OS data was presented at WCLC'18 and showed a compelling HR of 0.68 (concurrently published in NEJM). About 30% of NSCLC patients are diagnosed with early-stage disease about half of which is unresectable. AZN has indicated that about half of PACIFIC-eligible patients are now getting Imfinzi which has become standard-of-care in this setting. The majority of KOLs surveyed at our March 2019 Health Care Conference believed that penetration would reach >75% of eligible patients within 2-3 years. AZN has benefited from the penetration ramp with NSCLC generating the majority of Imfinzi revenues. AZN has five additional (neo)adjuvant Phase III NSCLC trials ongoing with readouts between 2020 and 2023.

Despite its success in Stage III NSCLC, Imfinzi has yet to post positive results in the front-line metastatic setting. In July 2017, AZN announced that the combination of durvalumab + tremelimumab missed the PFS co-primary endpoint in the pivotal Phase III MYSTIC trial in 1L NSCLC (HR=1.05). In November 2018, AZN announced that durvalumab + tremelimumab missed OS vs. chemo (second co-primary endpoint; HR=0.85). However, Imfinzi monotherapy hit OS (HR=0.76, p=0.036), but with less survival benefit (16.3 months mOS) vs. Keytruda monotherapy (17.7 months mOS) in a similar patient population (PD-L1 expression 20-25%). In August 2019, it was announced that Phase III NEPTUNE, assessing Imfinzi+tremelimumab vs. chemotherapy in 1L NSCLC with blood TMB ≥20mut/Mb also failed to meet its primary endpoint of OS. We await other Imfinzi opportunities in 1L NSCLC with Phase III PEARL (Imfinzi monotherapy) and POSEIDON (Imfinzi+treme+chemo). POSEIDON posted topline positive PFS in October 2019, but OS data have not yet matured (expected H1:20).

Durvalumab Approved In 2L Bladder

In May 2017, Imfinzi (durvalumab) received accelerated approval for the treatment of 2L bladder cancer post platinum chemo (before or after surgery), regardless of PD-L1 expression. The approval was based on Phase I/II Study 1108, in which Imfinzi reported an ORR of 20.4% in all patients and 29.5% in PD-L1 high-expressers (>/=25%); the ORR in PD-L1- patients was 7.7%. Approximately 15.5% of evaluable patients achieved partial response and 4.9% achieved complete response. SAEs occurred in 46% of patients; the most frequent were acute kidney injury (4.9%), UTI (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%), and general health deterioration (3.3%). Imfinzi was discontinued in 3.3% of patients.

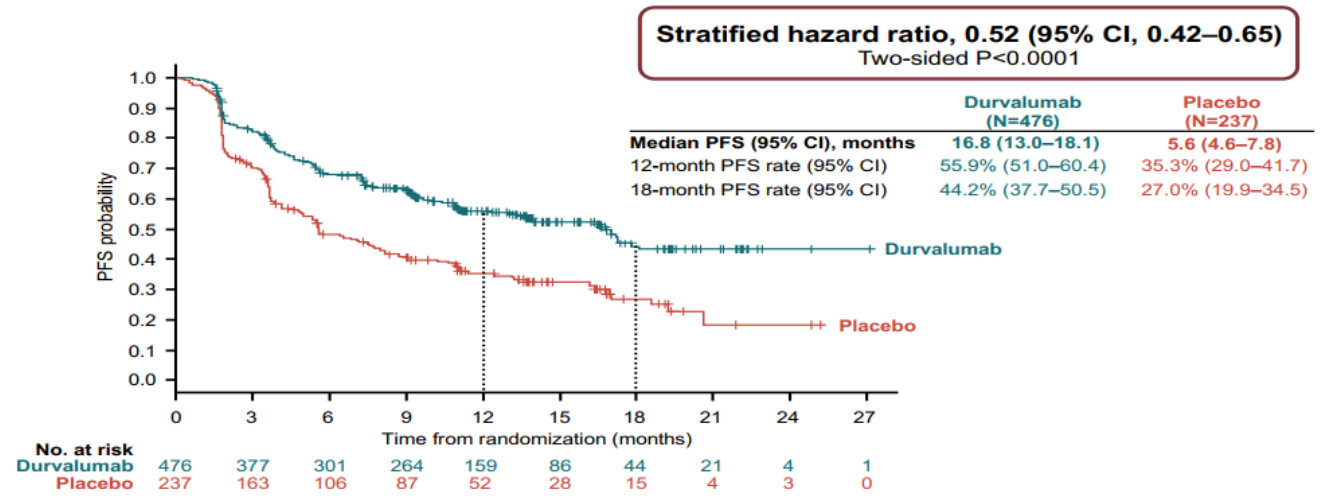
In the IO bladder market, Astra joined Roche (2L approved May 2016, 1L approved April 2017), Bristol (2L approved February 2017) and Merck (1L and 2L approved May 2017; hit OS). AZN initiated the Phase III DANUBE trial in September 2015, to assess Imfinzi +/- tremelimumab in 1L bladder (data expected in 2019). In 2018, AZN initiated 2 new pivotal Phase III bladder cancer trials. Phase III NILE initiated in September 2018 and will test Imfinzi+chemo, vs. Imfinzi+treme+chemo, vs. chemo in 1L bladder cancer. NILE primary completion is expected in April 2022, on PFS and OS co-primary endpoints. Phase III NIAGARA initiated in November 2018 and will evaluate neoadjuvant Imfinzi+chemo followed by adjuvant Imfinzi in early-stage bladder cancer. NIAGARA primary completion is expected in December 2025, on pCR and EFS co-primary endpoints.

PACIFIC Regimen Now Standard Of Care In Unresectable Stage III NSCLC

In May 2017, Astra announced positive results for PACIFIC, a Phase III trial of Imfinzi in patients with locally advanced, unresectable Stage III NSCLC who had not progressed following standard platinum-based chemotherapy/radiation. Astra states that stage III lung cancer represents about one-third of NSCLC or around 100,000 patients in the U.S. About half of these patients have tumors that are unresectable. Interim data was presented at ESMO in September 2017 and published in the NEJM in November 2017, demonstrating Imfinzi significantly improved the PFS co-primary endpoint (mPFS=16.8 months) versus placebo (mPFS=5.6 months, p<0.001). While OS was ongoing at the time, the 18-month ongoing response was 73% for Imfinzi (28.4% ORR) vs. 47% for placebo (16.0% ORR). Based on impressive PFS data, and despite awaiting OS, the FDA granted approval for Imfinzi in adjuvant treatment of unresectable Stage III NSCLC in February 2018. In May 2018, AZN announced Imfinzi hit OS in PACIFIC with data presented at IASLC in September 2018. OS, a second primary endpoint, showed a HR of 0.68 (p=0.0025). Imfinzi was approved in Japan in July 2018 for unresectable Stage III NSCLC and in China in December 2019. EU approval was granted in September 2018 although only for patients with PD-L1 expression of 1% or greater; management does not agree with the post-hoc exploratory subgroup analysis that was done to determine this limitation, as PACIFIC was all-comers and was not intended to treat patients by PD-L1 status. At ASCO'19, three-year OS data for PACIFIC were provided. Median survival and OS rates at 12, 24 and 36 months were estimated by Kaplan-Meier method with data cutoff at Jan. 31, 2019. Updated OS remained consistent with that previously reported (stratified HR 0.69, 95% CI, 0.55–0.86), with Imfinzi median not reached (NR; 95% CI, 38.4 months–NR) vs. 29.1 months (95% CI, 22.1–35.1) for placebo. 12-, 24- and 36-month OS rates with Imfinzi vs. placebo were 83.1% vs. 74.6%, 66.3% vs. 55.3%, and 57.0% vs. 43.5%. After discontinuation, 43.3% and 57.8% in the Imfinzi and placebo groups, respectively, received subsequent therapy. Of these, 9.7% and 26.6% received subsequent immunotherapy. These data demonstrate substantial long-term benefits with Imfinzi that further entrench the drug in Stage III unresectable NSCLC and raise the bar for competitors.

With PACIFIC, Imfinzi became the second PD-1/PD-L1 inhibitor to be approved in the localized/adjuvant setting (BMY's Opdivo approved for adjuvant melanoma in December 2017). BMY, MRK, and Roche each have Phase II data in Stage III lung cancer, but sentiment is that NCCN is unlikely to include other agents in compendia based on these small datasets. In April 2019, MRK received approval for Keytruda monotherapy in Stage III unresectable NSCLC based on KEYNOTE-042, but only in patients ineligible for chemoradiation, a much smaller, non-overlapping group relative to the PACIFIC regimen.

PACIFIC – PFS By BICR (Blinded Independent Central Review)



Source: AstraZeneca ESMO 2017

Despite MYSTIC failure (see below), we assume that AZN will gain 3% share of the PD-1/PD-L1 market in advanced metastatic lung cancer by 2025. Accounting for PACIFIC, AZN's five ongoing (neo)adjuvant Phase III NSCLC trials, and entry of competition, we assume that AZN will hold 55% share of the PD-1/PD-L1 market in localized/adjuvant NSCLC by 2025.

CASPIAN: Positive Results For Imfinzi+Chemo In SCLC Will Add An Important Indication; Priority Review Granted November 2019

On June 27, 2019, AZN reported that the Imfinzi+chemo arm of Phase III CASPIAN, examining Imfinzi+chemo with or without tremelimumab in 1L extensive stage SCLC, achieved OS vs. chemo alone. Orphan drug designation was then granted by the FDA in July 2019 and Priority Review was announced after filing in November; PDUFA is in Q1:20. Data were presented at WCLC in September 2019 showing that Imfinzi+chemo yielded mOS of 13.0 months vs. 10.3 months for the chemo only arm (HR 0.73, 95% CI 0.59-0.91). OS rate at 18 months was 33.9% vs. 24.7%. PFS HR was 0.78 (95% CI 0.65-0.94) but mPFS for Imfinzi+chemo was actually shorter than control (5.1mo vs. 5.4mo). Landmark PFS at 12 months, however, was 17.5% vs. 4.7% indicating a longer tail to the response curve with IO, as has been seen in other studies. ORR was 67.9% for Imfinzi+chemo vs. 57.6% for chemo alone. This release makes AZN the second company to post positive data in 1L SCLC amid relatively low expectations given past IO failures and the aggressiveness of the cancer. The same indication has proven valuable for Roche with strong uptake after its groundbreaking approval based on IMPOWER133 in Q1:19. AZN's results look very similar to IMPOWER133 with slightly better mOS benefit for Imfinzi (13 vs. 10.3) relative to Tecentriq (12.3 vs. 10.3) but OS HR being slightly worse (0.73 for Imfinzi vs. 0.70 for Tecentriq). Imfinzi looked slightly worse on PFS as

well. Differences in trial design provide some important additional competitive insights. The chemo comparator arm in CASPIAN was up to 6 cycles, same as used in practice. IMPOWER133 provided relatively modest OS benefit (~2mo) and no ORR benefit despite a chemo comparator arm that only used 4 cycles. So, there was a relatively low bar, and AZN is likely to be competitive in this tumor type. However, the Imfinzi+treme+chemo arm of CASPIAN did not apparently reach significance at this interim readout. Primary completion for the trial was September 30, 2019.

MYSTIC And NEPTUNE: Imfinzi + Treme Fails In 1L NSCLC

In July 2017, Astra announced that Imfinzi plus tremelimumab in MYSTIC (n=1,092) did not meet its primary endpoint of PFS compared to chemotherapy in patients with PD-L1 expression of 25% or greater. The secondary endpoint of Imfinzi monotherapy (although not formally tested since primary endpoint failed) also would not have met PFS. At the time, the trial continued in order to assess two remaining primary endpoints of OS for the Imfinzi+treme combo and for Imfinzi monotherapy.In November 2018, AZN announced that the treatment of durvalumab + tremelimumab missed OS vs. chemo (second co-primary endpoint; HR=0.85). However, Imfinzi monotherapy did hit OS in PD-L1 selected patients (tumor cell expression ≥25%). Data were presented at WCLC 2018, and median OS was 16.3 months for Imfinzi-alone vs. 12.9 months for chemotherapy (HR=0.76, p=0.036). The 24-month OS rate was 38.3% for Imfinzi-alone vs. 22.7% for chemotherapy. As part of a post-mortem, AZN performed a retrospective analysis for TMB in MYSTIC. Blood (bTMB) and tissue (tTMB) tumor mutational burden were examined to determine predictive value for drug response. Both measures were positively associated with efficacy; Imfinzi+tremelimumab-treated patients with bTMB ≥20mut/Mb or tTMB ≥10mut/Mb exhibited mOS of 21.9 and 16.6 months, respectively, compared to 8.5 and 8.4 months for those with mut/Mb below the cutoffs. According to AZN, this represented the most comprehensive data set examined to date supporting TMB as a predictive biomarker for checkpoint inhibitors.

These data provided a rationale for selecting Phase III NEPTUNE 1L NSCLC patients based on bTMB ≥20mut/Mb regardless of PD-L1 expression levels. The trial assessed Imfinzi+treme vs. chemotherapy but it was announced in August 2019 that NEPTUNE failed on OS. With BMY having stated in July that they discontinued pursuit of TMB for patient stratification of CM-227 in 1L NSCLC, it appears that this biomarker hypothesis may be settled.

Imfinzi also failed in 3L NSCLC (Phase III ARCTIC, announced April 2018) but has upcoming opportunities beyond MYSTIC and NEPTUNE for Imfinzi in 1L NSCLC, with Phase III POSEIDON (Imfinzi + chemo +/- treme, vs. chemo; estimated primary completion in September 2019), and Phase III PEARL (vs. chemo, pre-dominantly Asian; estimated primary completion in September 2019).

POSEIDON Has Not Yet Achieved OS But Chances Of Role In 1L NSCLC Somewhat Improved With PFS Win

AZN announced in October 2019 that Ph III POSEIDON, testing Imfinzi+chemo or Imfinzi+tremelimumab+chemo vs. chemo in 1L NSCLC met a co-primary endpoint of progression-free survival at final analysis. Overall survival, potentially needed for filing, continues to be tracked with data expected in 2020. This positive result was made somewhat less surprising by CM-9LA's favorable readout a week prior (BMY, testing Opdivo+Yervoy+chemo triplet), but OS outcomes are still needed to determine whether POSEIDON is approvable, let alone competitive. Data have not yet been released, but inferences can be drawn regarding efficacy and safety. On efficacy, the statistical plan has not been outlined, but it was confirmed that this was the final analysis of PFS. It is unclear if there was an interim analysis in which the OS coprimary endpoint was not

met, but median follow-up was ~12 months which is longer than that needed to yield significant OS for the Keytruda (MRK) regimens although possibly shorter than the CM-9LA interim readout. AZN noted that they are "sharing" results with health authorities, but OS may be needed for registration. Although both Imfinzi+chemo and Imfinzi+treme+chemo hit PFS, it is not known if treme provided additive benefit. Still, this news modestly increases the probability that Imfinzi could see approval in front-line lung cancer, and that tremelimumab might reach the market. On safety, AZN stated that the Imfinzi+chemo and Imfinzi+treme+chemo arms exhibited comparable safety. Pending full data, this could remove one hurdle to the use of the IO/ IO/chemo triplet as IO/chemo doublets have manageable safety profiles. It is possible, however, that comparable safety in the two arms belies poor activity of tremelimumab which has not yet shown significant clinical benefit in any late stage trial.

ARCTIC A Final Setback For Imfinzi+Tremelimumab In 3L NSCLC

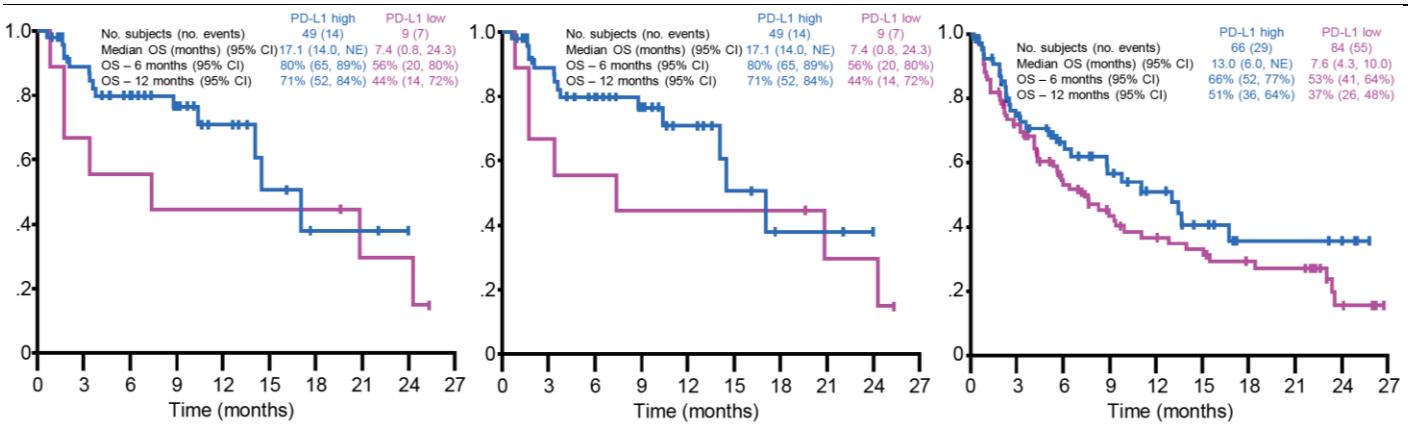
The Phase III ARCTIC trial was a randomized, open-label study to evaluate Imfinzi+treme, as well as Imfinzi and treme monotherapies, vs. chemotherapy in metastatic NSCLC patients, who have received at least 2 prior lines of therapy. The trial contains 2 sub-studies: sub-study A (Imfinzi monotherapy vs. chemo in patients with high PD-L1 expression), and sub-study B (Imfinzi mono, treme mono, Imfinzi+treme, vs. chemo in patients with low/negative PD-L1 expression; randomized 2:1:3:2, respectively). Only sub-study B was powered for statistical significance, but in April 2018 AZN announced that sub-study B treatment of Imfinzi+treme failed to demonstrate statistical significance vs. chemo for both co-primary endpoints of PFS and OS. ARCTIC marks the second 3L failure after Phase II ATLANTIC.

Initial Data For Durvalumab Monotherapy In NSCLC Encouraging, But Faltered In Phase II For 3L Treatment

At ESMO:16, Astra presented updated Phase I/II data showing response rate of 18% (50/285) in patients with advanced NSCLC treated with durvalumab. Antitumor activity was observed across histology, line of therapy and PD-L1 expression. Response rate was 21%/14% in squamous/non-squamous, 27%/19%/13% in first/second/third line and 25%/6% in PD-L1+/PD-L1- patients. In first line, mOS was 17 months for PD-L1+ patients and 7 months for PD-L1- patients. This compares with historical ~12 months of mOS for platinum-based chemotherapy. Early durvalumab data was on par with data from Opdivo and Keytruda, which showed response rates of 15-20% in similar studies.

At ASCO:16, data from a small cohort of treatment naïve patients showed response rate of 27% (16/59) in patients with advanced NSCLC treated with durvalumab. Response rate was 29% (14/49) in PD-L1+ patients and 11% (1/9) in PD-L1- patients. No responses were observed in patients who were never smokers. Responses were observed in both squamous and non-squamous histology. Durvalumab was fairly well tolerated with only 7% (4/59) of patients experiencing an AE leading to discontinuation but one death of pneumonitis was reported.

OS Curves For Patients With NSCLC Treated With Durvalumab In First Line (Left), Second Line (Middle) And Third+ Line (Right)



Source: Company data

At WCLC:16, full Phase II data from ATLANTIC were presented. The study enrolled a highly refractory population that received 2.6-3.2 prior lines of therapy. In the study, durvalumab delivered response rate of 7.5% (7/93) in patients expressing PD-L1<25%, 16.4% (24/146) in patients expressing PD-L1>25% and 30.9% in patients expressing PD-L1>90%. Longitudinal outcomes (PFS/OS) were unimpressive but are of limited interpretability given the severity of the population enrolled. Astra originally planned to file durvalumab monotherapy in lung based on response rates from ATLANTIC. However, as the competitive standard evolved to include survival benefit, ATLANTIC PFS/OS could not measure up for a clear approval pathway.

Mesothelioma Data Promising

At ASCO 2018, updated data from the Phase II DREAM trial in mesothelioma was presented. 54 chemo-naive patients with all histologies of malignant pleural mesothelioma (MPM) were evaluated for the addition of Imfinzi with 1L chemotherapy (31 pts in Stage I, 23 pts in Stage II). In the first 31 evaluable patients of Stage I, 65% achieved the primary endpoint for 6-month PFS, with an mPFS of 7.3 months. Confirmed ORR was 58% by iRECIST (0 CRs, 18 PRs, 9 SD), 20 patients (65%) experienced grade 3+ AEs with neutropenia (16%) and nausea (13%) being the most common.

MPM contributes to over 38,000 deaths/year worldwide, and remains an unmet need, evidenced by rapid recruitment in the study. The current treatment paradigm in 1L is cisplatin/carboplatin + pemetrexed for 4-6 cycles resulting in 6-month PFS of about 65%, 12-month PFS of about 12%, ORR of about 41%, and mOS of about 12 months. Previous studies combining chemo+Avastin have increased mPFS to 9.2 months (vs. 7.3 months on chemo) and mOS to 18.8 months (vs. 16.1 months on chemo) but did not report ORR. PD-L1 expression in mesothelioma is reported to be 20-70%, providing rationale for the combination of PD-1/PD-L1 inhibitors. A 58% confirmed ORR in this study is impressive, could lead to improvements in mPFS, and should support follow-up studies for longer durations and OS.

Early Data In TNBC

Data from the Phase II GeparNuevo trial (NCT02685059) in neoadjuvant TNBC was presented at ASCO 2018. 174 TNBC patients were stratified by stromal tumor infiltrating lymphocytes (sTILs; low 0-10%, medium 11-59%, and high 60-100%), then randomized 1:1 to receive either Imfinzi+chemo or placebo+chemo. In addition, two

thirds of patients (n=117) also received Imfinzi neoadjuvant monotherapy for 2 weeks prior to starting their Imfinzi+chemo or chemo regimens. The primary endpoint was pathological complete response (pCR). Overall, patients receiving Imfinzi demonstrated a 53.4% pCR versus 44.2% with placebo, which was numerically higher but not statistically different (p = 0.287). However, patients receiving Imfinzi neoadjuvant therapy generated a more Imfinzi-favorable pCR odds ratio of 2.22 (p = 0.035) vs. those who did not receive neoadjuvant therapy with a pCR odds ratio of 0.611 (p = 0.36).

There are several neoadjuvant and adjuvant trials under way using PD-1/ PD-L1 inhibitors in TNBC: MRK (Phase III KN-522); RHHBY (Phase III IMpassion031); and PFE (Phase III A-Brave). KN-522 posted a significant improvement in pCR rates that will likely see Keytruda approved in the neoadjuvant TNBC setting as early as 2020.

Tremelimumab Combo Strategy In Question After Multiple Failures; POSEIDON Offers Near-Term Path To Potential Approval

Tremelimumab is an anti-CTLA4 mAb in Phase II/III studies across solid tumors with safety and efficacy data in >1,000 patients. Although not yet approved in any indication, its potential success hinges on combination with durvalumab. In monotherapy, tremelimumab was granted FDA Orphan Drug status in mesothelioma. However, in February 2016, AstraZeneca announced that the Phase IIb registrational trial DETERMINE (n=500+), in platinum refractory mesothelioma, did not meet the OS endpoint. Full data at ASCO 2016 showed almost perfectly superimposable curves with mOS of 7.7 months for tremelimumab vs. 7.3 months for placebo (HR=0.92), 18-months OS of 17% for tremelimumab vs. 18% for placebo and no subgroups drawing a benefit.

Nonetheless, AstraZeneca remains optimistic for tremelimumab in combination with other agents, such as durvalumab. In addition to the NSCLC POSEIDON trial described above, AZN is also evaluating the Imfinzi+treme combo in Phase III trials for bladder (i.e. DANUBE, NILE, NIAGARA; described above), HCC (i.e. HIMALAYA), and head & neck cancer (i.e. KESTREL in 1L). Phase III CASPIAN, assessing durvalumab ± treme + chemo vs. chemo in 1L SCLC, reported positive results for the +chemo arm (see above) but combination with treme does not yet appear to have added benefit though the study is ongoing. Imfinzi+treme combinations have already failed several Phase III trials including in 1L NSCLC and 2L HNSCC. We estimate tremelimumab sales of $15MM in 2020, and $350MM in 2025.

Phase II CONDOR Provided First Data In H&N Cancer

In February 2018, AZN announced data from the Phase II CONDOR study at the Multidisciplinary Head and Neck Cancers Symposium. AZN previously has stated that this trial was not registrational given that competitive agents are approved on OS in all-comers. CONDOR compared Imfinzi, Tremelimumab, and Imfinzi+treme in patients with recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC). The target population was defined as PD-L1 low/negative patients (cut-off for inclusion was less-than 25% TC). The primary endpoint was ORR, and secondary endpoints included OS and PFS for combination vs. monotherapies. Imfinzi alone demonstrated the highest ORR at 9.2% (n=6 of 65), albeit with a broad confidence interval (95% CI: 3.5-19.0). Treme demonstrated the lowest ORR at 1.6% (n=1 of 63; 95% CI: 0.04-8.5), and the Imfinzi+treme combo an ORR of 7.8% (n=10 of 129; 95% CI: 3.8-13.8). Median PFS was similar across groups: 1.9 months for Imfinzi mono, 1.9 months for Treme mono, and 2.0 months for the combo. Median OS appeared slightly better for the combo (7.6 months) vs. Imfinzi mono (6.0 months) and Treme mono (5.5 months), but a full statistical analysis was not provided. Percent survival at 12 months was similar for both combo and Imfinzi mono (both ~37%), which were higher than Treme mono (~25%).

In December 2018, AZN announced that both Imfinzi-alone and Imfinzi + treme failed to hit OS vs. SOC in the Phase III EAGLE trial for 2L HNSCC. We expect data from the Phase III KESTREL trial in 1L HNSCC (Imfinzi + treme vs. SOC) in H1:20.

In second line, AZN had flagged Phase III EAGLE as potentially registrational, evaluating Imfinzi +/- treme vs. standard of care therapy. In December 2018, however, AZN announced that both Imfinzi-alone and Imfinzi + treme failed to hit OS vs. SOC. EAGLE data were presented at ASCO'19 showing mOS for Imfinzi, Imfinzi+treme, and SOC of 7.6mo (95% CI 6.1-9.8mo), 6.5mo (95% CI 5.5-8.2mo), and 8.3mo (95% CI 7.3-9.2).

Gastric Cancer Data In Treme/Imfinzi Combo Positive

Data from the Phase Ib/II trial evaluating Imfinzi+treme for the treatment of 2L+ advanced gastric cancer was presented at ASCO 2018. 2L patients were randomized 2:2:1 to Imfinzi+treme, Imfinzi-alone, or treme alone. 3L patients received Imfinzi+treme. As of September 2017, 58 patients received Imfinzi+treme (9.2-month follow-up), 24 received Imfinzi monotherapy (3.5-month follow-up), and 12 received treme monotherapy (9.2-month follow-up). The median for primary endpoint of PFS in 2L Imfinzi +treme was 1.8 months, vs. 2L Imfinzi-alone at 1.6 months, vs. 2L treme-alone at 1.7 months, vs. 3L Imfinzi+treme at 1.8 months. However, the median for secondary endpoint of OS in 2L Imfinzi+treme was 9.2 months, vs. 2L Imfinzi-alone at 3.2 months, vs. 2L treme alone at 7.7 months, vs. 3L Imfinzi+treme at 10.6 months.

Data was similar across PD-L1 expression groups. mOS for Imfinzi+treme in PD-L1 low/negative patients in 2L (8.9 months) and 3L (10.6 months) outperformed treme monotherapy (5.6 months). Imfinzi+treme and treme-alone demonstrated higher rates of confirmed response and 6-month PFS versus Imfinzi monotherapy, but the presenter noted that Imfinzi-alone likely underperformed due to a higher enrollment of poor-prognostic patients in that arm. Data for OS was encouraging, but ORR scores for the combo (7.4% confirmed overall, 14.3% confirmed for high PD-L1 patients) appeared to be somewhat lower than what has been reported for Opdivo+Yervoy in 2L gastric cancer (12-24%). Tails of the OS curves for the combination in 2L and 3L suggest that the PD-L1/ CTLA4 combo had an additive effect, while the combo had less grade 3+ TRAEs (28.8%) and discontinuations (17.3%) vs. treme-alone (grade 3+ TRAEs: 50.0%; discontinuations: 33.3%).

Growing List Of Collaborations For Durvalumab, Other Agents

Advaxis — In July 2014, Astra announced a collaboration with Advaxis to evaluate MEDI4736 + ADXS-HPV, Advaxis' lead cancer immunotherapy vaccine, as treatment for advanced, recurrent, or refractory HPV-associated cervical cancer and HPV-associated squamous cell carcinoma of the head and neck. Pre-clinical work has suggested that ADX-HPV combined with a checkpoint inhibitor can enhance anti-tumor response. The Phase I (dose) and Phase II (safety) portions of the trial will be funded and conducted by Advaxis. Results will inform further efforts. The collaboration is non-exclusive for HPV-driven tumors, with Astra having first right of negotiation for future development combos involving durvalumab. The Phase I/II initiated in April 2015, but a clinical hold was placed on the trial after a patient death due to respiratory failure. The trial is currently suspended.

Bavarian Nordic – In February 2018, Bavarian Nordic announced a collaboration with AstraZeneca and Georgetown University for the evaluation of CV301 (IO agent that targets CEA and MUC1) plus durvalumab and maintenance chemo in 2L+ metastatic colorectal and pancreatic cancers. Both companies will fund the Phase I/II trial which started in November 2018. The non-randomized, open label study has an estimated

enrollment of 54 patients. The estimated primary completion is in December 2021 to evaluate dose and PFS co-primary endpoints.

Celgene — In April 2015, Astra announced a collaboration with Celgene for the development and commercialization of durvalumab (alone and in combo) for various blood cancers including NHL, myelodysplastic syndromes, and MM. Celgene paid Astra $450MM upfront, will lead clinical trials, pay for R&D costs until the end of 2016 (and then pay for 75% of R&D costs), and be responsible for global commercialization. Astra will be responsible for manufacturing, book all sales, and pay Celgene a royalty on WW sales for hematological applications of 70% to start, decreasing to roughly 50% in four years. Bristol's acquisition of Celgene, expected to close in late 2019/early 2020, leaves the future of this collaboration uncertain.

Eli Lilly – In May 2015, Astra announced a collaboration with Eli Lilly to evaluate durvalumab + Cyramza (ramucirumab) in advanced solid tumors. LLY will sponsor the trials. A Phase I study for the combination initiated in March 2016. The study enrolled 114 patients. Data from the gastric cancer cohort showed promising antitumor activity.

Foundation Medicine – In June 2016, Astra entered into a collaboration with Foundation Medicine to develop companion diagnostic assays that can be utilized to identify patients most likely to benefit from Astra's pipeline of oncology agents. Terms of the collaboration were not disclosed. In July 2019, the FoundationOne CDx companion diagnostic for olaparib for BRCAm ovarian cancer was approved.

Immunocore — In April 2015, Astra announced a clinical trial collaboration with privately-held Immunocore to evaluate durvalumab and/or tremelimumab with IMCgp100, Immunocore's lead T-cell receptor-based agent, in metastatic melanoma. Immunocore will conduct the Phase Ib/II trials. Astra will have exclusive rights to the combos and first rights of negotiation for commercialization of these combos in other tumors. This agreement expands a January 2014 research and licensing agreement with Immunocore. In January 2016, IMCgp100 was granted Orphan Drug Designation for uveal melanoma and subsequently Fast Track Designation in April 2019.

ImmunoMedics - In July 2018, Astra announced a collaboration with Immunomedics to evaluate Imfinzi + ADC sacituzumab govitecan in 1L TNBC and 1L urothelial cancer. The Phase I/II studies will be co-funded by the two companies. In November 2018, the collaboration was expanded to include 2L NSCLC. We expect these trials to initiate in 2019.

Incyte — In May 2014, Astra entered into a non-exclusive collaboration with Incyte to evaluate durvalumab plus Incyte's IDO1 inhibitor epacadostat (INCB24360) in multiple solid tumors including melanoma, NSCLC, SCCHN, and pancreatic cancer. In January 2016, the agreement was expanded to include Tagrisso + Incyte's JAK1 inhibitor (INCB39110) in EGFR+ NSCLC patients who have developed a resistance to 1st-gen TKI inhibitors; a Phase I/II study will be conducted by Incyte. In October 2017, an exclusive collaboration was announced for a Phase III trial of epacadostat + Imfinzi in Stage III unresectable NSCLC. Following the failure of the Phase III ECHO-301 trial evaluating epacadostat + Keytruda (MRK) in advanced melanoma in April 2018, Incyte overhauled its clinical program by suspending 6 of the 8 remaining Phase III trials (including the suspension of the Phase III PACIFIC-3 trial evaluating Imfinzi + epacadostat). The 2 Phase III combination trials that were not suspended (Keytruda + epacadostat, in NSCLC), will continue as Phase II trials. Additional trials of epacadostat + Imfinzi have not been pursued.

Innate Pharma — In April 2015, Astra announced a collaboration with Innate Pharma to develop Innate's monalizumab/IPH2201 (anti-NKG2A) as monotherapy and in combo with durvalumab. Astra paid Innate $250MM upfront and will pay $100MM prior to the initiation of Phase III studies, and additional undisclosed milestone payments up to a potential $1.275B. Astra will book all future sales and pay Innate a double-digit royalty on net sales; in Europe, Innate may co-promote with Astra and equally share profits. In January 2018, the collaboration added the combination of IPH5401 (anti-C5aR) plus durvalumab; a Phase I in solid tumors initiated in September 2018. In October 2018, the collaboration was expanded with Astra gaining full rights to monalizumab as well as option rights to in-license IPH5201 (CD39 antibody) as well as four other preclinical molecules.

Monalizumab is also being studied with cetuximab (anti-EGFR mAb; LLY) in recurrent or metastatic H&N cancer, for which data from a single-arm Phase II trial was presented at ESMO 2018. In 40 evaluable patients, the combination of monalizumab + cetuximab demonstrated an ORR of 27.5% (CR=2.5%, PR=25%), with an mDOR of 5.6 months. The median PFS was 5.0 months, and median OS was 10.3 months. In a subgroup analysis presented at SITC 2018, there were 23/40 IO-naïve patients and 17/40 IO pre-treated patients. In IO-naïve, ORR was increased to 35%, mDOR was 5.3 months, mPFS decreased to 4.0 months, and mOS was consistent at 10.3 months. In IO pre-treated patients, ORR decreased to 18%, mDOR was 5.6 months, mPFS was consistent at 5.0 months, and mOS increased to 12.8 months. In September 2019, Innate announced that a Phase III trial of the combo in SCCHN will start in 2020.

Inovio — In August 2015, Astra announced a collaboration with Inovio to acquire the exclusive rights to T-cell activating HPV cancer vaccine MEDI0457 (INO-3112), in Phase I/II for cervical and head and neck cancers (caused by HPV types 16 and 18). At ASCO'18, AZN reported early interim results from this Phase I/II trial for 10 patients evaluated as of January 23, 2018 (n=7 newly-diagnosed inoperable patients; n=3 recurrent disease patients). Of the newly-diagnosed cohort, 4 of 7 demonstrated Interferon-g (IFNg) secretion response. Of the recurrent disease cohort, 0 of 3 had IFNg response. Immuno-responses against HPV oncoproteins were detected in 60% of patients: 5 pts with anti-HPV16 E6, 4 pts with anti-HPV16 E7, 3 pts with anti-HPV18 E6, and 6 pts with anti-HPV18 E7. TRAEs were all grade 1, all C1 patients alive at 60 weeks. Astra paid $27.5MM upfront and will pay up to $700MM in milestone payments, all development costs, and double-digit tiered royalties. Astra and Inovio had agreed to develop up to two additional DNA-based cancer vaccines not in the current pipeline, but in May 2019, Astra announced it would restrict the collaboration to INO-3112 moving forward.

Kyowa Hakko Kirin — Announced in July 2014, the collaboration will evaluate durvalumab + mogamulizumab (anti-CCR4) and also mogamulizumab + tremelimumab. The studies will be co-funded, and Kyowa will conduct the trials. Data from a Phase II trial evaluating mogamulizumab in combination with either Imfinzi or treme in solid tumors (NCT02301130) was shown at SITC'18; efficacy was reported as promising with biomarkers of immune effects aligned with treatment response.

Moderna – In 2013, AZN and Moderna Therapeutics entered into a collaboration to develop potential agents for use in cardiovascular, metabolic, and renal diseases. In January 2016, Astra expanded an existing collaboration with Moderna Therapeutics to include development and commercialization of Moderna's messenger RNA candidates for a range of cancers. With the updated agreement, the companies will collaborate on two specific IO programs. In August 2016, Astra increased its equity interest in Moderna with a $140MM preferred stock investment, resulting in an approximately 9% ownership position.

The first candidate (AZD8601) is an investigational mRNA-based therapy that encodes for vascular endothelial growth factor-A. It entered Phase I for Type 2 diabetes mellitus in Germany (n=44), initiating in December 2016. Moderna announced that the trial completed in January 2018, meeting its primary safety and secondary proof-of-mechanism endpoints. Moderna initiated a Phase IIa trial in the EU (n=33), for the treatment of heart failure in patients undergoing CABG. The estimated primary endpoint completion is in July 2020, assessing 10 primary outcomes including AEs/SAEs, ECGs, LV ejection fraction, physical examination, blood pressure, pulse, hematology, clinical chemistries, and urinalysis.

In November 2017, the companies announced a license and collaboration agreement to co-develop and co-commercialize AZD7970, an mRNA therapeutic encoding Relaxin, for the treatment of heart failure. AZN is responsible for early clinical development, and both companies will share costs of late-stage clinical development. U.S. commercialization of AZD7970 is structured in a 50:50 profit sharing arrangement. AZN will lead ex-US efforts, with Moderna receiving tiered royalties. As of Q1:2019, no clinical trials had been announced or initiated for AZD7970.

Pharmacyclics/AbbVie — In November 2014, Astra announced a clinical trial collaboration with Pharmacyclics/AbbVie to evaluate Imbruvica (oral TKI) with durvalumab in solid tumors. A second collaboration will evaluate two of Astra's PI3 inhibitors with Imbruvica in relapsed/refractory DBCL. The agreement is non-exclusive and may include multiple Phase I/II studies. The solid tumor studies will be led by AbbVie, and the hematological cancer studies by Astra. Phase Ib/II studies of durvalumab + Imbruvica in r/r NSCLC, breast cancer, and pancreatic cancer were initiated in April 2015, as part of a single multi-center study in patients with r/r solid tumors (NCT02403271). The study enrolled 124 patients and completed in August 2017.

In June 2018, results from the Phase I/II were presented at ASCO'18. In 49 patients with Stage III/IV pancreatic cancer, mPFS was 2 months, mOS was 4 months, and DOR was 10 months. In 45 patients with Stage III/IV HER2+ TNBC, mPFS was 2 months, mOS was 4 months, and DOR was 23 months. In 28 patients with Stage III/IV NSCLC, mPFS was 2 months, mOS was 8 months, and DOR had not been determined.

Lynparza Gains Approval Beyond BRCAm Cancers

Lynparza (olaparib/AZD2281) is an oral inhibitor of poly-ADP-ribose polymerase (PARP), an enzyme involved in DNA repair. BRCA mutated cancers have increased reliance on PARP to repair their DNA and continue to divide. PARP inhibitors have shown impressive efficacy in BRCA mutated cancers. Tumors with other homologous recombination repair deficiencies (HRD) have also been shown to be responsive to PARP inhibition. Some data suggest that these agents can be found clinically relevant beyond BRCA and HRD, especially when combined with other mechanisms (DDR inhibitors, IO, anti-angiogenic agents, Akt inhibitors, etc.). Lynparza has been approved in ovarian (US, EU 2014, Japan, China 2019), breast (US 2018; EU 2019), and pancreatic cancer (US 2019); approval in prostate cancer is expected in 2020. Studies in gastric cancer failed to show a benefit. Lynparza is being co-developed and co-commercialized with Merck, an agreement announced in July 2017. Combinations with the companies' respective PD-(L)1 inhibitors are excluded from the partnership. Merck paid Astra $1.6B upfront, $750MM for certain license options, and up to $6.15B for regulatory (one-third) and sales (two-thirds) milestones (deal included selumetinib). Astra books all sales of Lynparza and selumetinib. The deal is not exclusive on either side, and there are no tumor-specific carve outs. We estimate Lynparza sales of $1.2B (+85%) in 2019, $1.71B in 2020, and $4.05B in 2025.

SOLO-1 Data In 1L Ovarian Impressive

At ESMO 2018, Astra presented full date from the Phase III SOLO-1 (n=391) trial in which newly diagnosed BRCA-mutated ovarian cancer patients were randomized 2:1 with Lynparza (n=260) vs. placebo (n=130). At a median follow-up of 41 months, median investigator assessed PFS (primary endpoint) had not been reached for Lynparza vs. 13.8 months on placebo (HR=0.30, p<0.0001), demonstrating Lynparza decreased risk of disease progression or death by 70%. Time to first subsequent therapy was 51.8 months on Lynparza vs. 15.1 months on placebo (HR=0.30, p<0.0001). Results demonstrate 60% of patients receiving Lynparza remained progression-free at three years compared to 27% on placebo following platinum-based chemotherapy. The most common grade 3+ toxicities with Lynparza were anemia (22%) and neutropenia (8%). Lynparza dose reductions, interruptions and discontinuations occurred in 28%, 52%, and 12%, respectively.

This data is a home run for Astra. At Cowen's 21st Annual Therapeutics Conference (October 2018), polled investors and specialists indicated they wanted to see ~10-15 months of PFS benefit vs. control. Our expert panelists did not view an absolute PFS benefit as the right metric for assessing the benefit in the frontline setting, but instead viewed a HR=0.5 or better (doubling of PFS) as the ideal target. While PFS has not yet been reached for the Lynparza cohort, the median follow-up of 41 months would suggest well more than a 10-15 month mPFS benefit vs. 13.8 months on placebo. More importantly, the PFS HR=0.30 surpasses the 0.5 expert threshold as a clinically meaningful result.

Lynparza Likely To Stay One Step Ahead In Ovarian Cancer With 1L PAOLA-1 Win

One month after GSK released positive top-line results from PRIMA, AZN announced in August 2019 that PAOLA-1 also achieved its primary endpoint in the front-line maintenance setting regardless of BRCA status. Data for both trials were presented at ESMO'19. Phase III PAOLA-1 (n=537) assessed the effect of Lynparza+Avastin vs. placebo+Avastin as maintenance therapy in platinum-sensitive front-line ovarian cancer patients. All Stage III patients were eligible. Investigator-assessed PFS in all-comers was the primary endpoint with pre-specified analysis of HRD subgroups (Myriad Mychoice assay score > 42 or BRCAm). In HRD patients, mPFS was 37.2 vs. 17.7 months with HR (95% CI) of 0.33 (0.25-0.45); in HRD-proficient patients, mPFS was 16.9 vs. 16.0 months with HR (95% CI) of 0.92 (0.72-1.17); and in all-comers, mPFS was 22.1 vs. 16.6 months with HR (95% CI) of 0.59 (0.49-0.72), p< 0.0001. Most common grade 3+ AEs were hypertension (19%), anemia (17%), lymphopenia (7%), and neutropenia (6%) with 20% leading to discontinuation.

These trials have likely earned PARP inhibitors a place in the SOC regimen. However, competitive dynamics between Lynparza and Zejula may not shift. We expect Lynparza to remain the leader in this indication with both Lynparza and Zejula likely to experience increased usage albeit in slightly different patient subgroups. PAOLA-1 should be an immediate boost to prescribing in 1L patients already eligible for Avastin maintenance therapy (less than 50% of patients) but the combination will likely only be used for HRD tumors (~50% of ovarian cancer overall). Dramatic PFS benefit from this trial could push physicians to use the combination in more patients than would otherwise have been considered for Avastin maintenance alone. Lynparza monotherapy in BRCAm patients is also likely to see an increase in prescribing (based on SOLO-1) as PARP inhibitors expand in the frontline. PRIMA represents Zejula's first positive registrational 1L data and will likely be used in patients regardless of HRD status, but primarily in those who have homologous recombination repair-proficient tumors and/or are poor candidates for Avastin. PRIMA posted a significant HR in HRD-negative patients, but it is important to recall that the comparator for this trial was placebo. When compared cross-trial,

HRD-negative patients receiving Zejula in PRIMA exhibited much lower mPFS (8.1mo) than Avastin-treated patients in PAOLA-1 (16.0mo). The discussant at ESMO suggested that sequencing PARP inhibition with Avastin maintenance could offer the best option but no trial has yet tested this hypothesis and in HRD tumors, it is difficult to argue with the robust effect of Lynparza's combination. On the safety side of the equation, the PAOLA-1 discontinuation rate was high, but hypertension, a known AE associated with Avastin, was actually lower with the combination. Zejula monotherapy carries its own risks, exhibiting much higher cytopenia rates than Lynparza+Avastin, and PRIMA posted a not insignificant discontinuation rate of 12%. More competitive data in ovarian cancer are expected with Zejula+Avastin maintenance being tested (Ph. III NCT03806049) and multiple trials with checkpoint inhibitor combinations (AZN's Imfinzi, MRK's Keytruda, and GSK's dostarlimab) are underway.

Lynparza vs. Zejula Efficacy In Ovarian Cancer

	LYNPARZA			ZEJULA		
	On Label		*Investigational*	*On Label*	*Investigational*	
Trial	**SOLO-1 (n=391)**	**SOLO-2 (n=295)**	**PAOLA-1 (n=806)**	**NOVA (n=553)**	**PRIMA (n=733)**	**PhII AVANOVA (n=97)**
Line	1L Maintenance	2L Maintenance	1L Maintenance	2L+ Maintenance	1L Maintenance	2L
Selection Markers	s or gBRCAm	gBRCAm	Pt-Sensitive	Pt-Sensitive	Pt-Sensitive	Pt-Sensitive
Combination	Monotherapy	Monotherapy	+Avastin	Monotherapy	Monotherapy	+Avastin
Comparator	Placebo	Placebo	Placebo+Avastin	Placebo	Placebo	Avastin Alone
mPFS (mo)	-	-	22.1 vs. 16.6	-	13.8 vs. 8.2	11.9
BRCAm	NR vs. 13.8	19.1 vs. 5.5	37.2 vs. 21.7	21.0 vs. 5.5	-	-
non-BRCAm	-	-	18.9 vs. 16.0	9.3 vs. 3.9	-	-
HRD	-	-	37.2 vs. 17.7	-	21.9 vs. 10.4	-
non-HRD	-	-	16.9 vs. 16.0	-	8.1 vs. 5.4	-
PFS HR (95% CI)	-	-	0.59 (0.49-0.72)	-	0.62 (0.50-0.76)	-
BRCAm	0.30 (0.23-0.41)	0.30 (0.22-0.41)	0.31 (0.20-0.47)	0.26 (0.17-0.41)	-	-
non-BRCAm	-	-	0.71 (0.58-0.88)	0.45 (0.34-0.61)	-	-
HRD	-	-	0.33 (0.25-0.45)	-	0.43 (0.31-0.59)	-
non-HRD	-	-	0.92 (0.72-1.17)	-	0.68 (0.49-0.94)	-

Source: Cowen and Company

Lynparza Granted Broad Maintenance Label In Ovarian Cancer

In August 2017, the FDA approved Lynparza for the maintenance treatment of platinum-sensitive recurrent ovarian cancer; similar approval was received in the EU in May 2018. The label is irrespective of BRCA status and essentially` mirrors niraparib's (Zejula) maintenance label. The broad approval was supported by both the recent Phase III SOLO-2 trial (gBRCA+ only) and the earlier Phase II Study 19 trial (all-comers), which had previously received a negative ODAC due to concerns surrounding the reliability of data from the small study size, side effects (both frequency of less severe side effects as well as potential for a few rare blood toxicities), lack of support for PFS as endpoint in maintenance setting by some panel members, and concerns that early approval may hinder finalization and reliability of the SOLO-2 study. Data from both studies are included in the new label and are consistent with previously reported data. Of note, the PFS data included for SOLO-2 is based on the primary investigator-assessed PFS and not central review, which reported a larger PFS benefit between olaparib and placebo. Also, Study 19 data in the label includes both PFS (investigator-assessed) and survival data suggestive of a survival benefit. The label reports a 2.0-month survival benefit for olaparib in the ITT, which translates to a 27% reduction in risk of death. No p-value is included as Astra previously reported that this trial failed to clear the high statistical hurdle of p<0.0095.

Safety data for olaparib's label are consistent with previously reported data. The label also reduces olaparib's pill burden to 4 pills/day from 16 pills/day. Taken together, olaparib's label expansion compares favorably to niraparib with similar PFS benefit in gBRCA+ patients (13.6 month for olaparib vs. 15.5 month for rucaparib), a potential

survival benefit claim, and a cleaner safety profile (niraparib requires weekly blood counts for first month). We continue to believe that the three PARPs are undifferentiated from an efficacy standpoint. In our view, niraparib continues to be the least well-tolerated PARP inhibitor in the maintenance setting, which our consultants have indicated will be of high importance given the expected duration of therapy.

SOLO 2 Data Solid In Ovarian Cancer; Competitive Advantage On Safety

In March 2017, SOLO-2 data were presented at the SGO meeting. SOLO-2 was a Phase III study evaluating olaparib (vs. placebo) in the 2nd/3rd-line maintenance setting in BRCA-mutant, platinum-sensitive ovarian cancer. SOLO-2 is very similar to Tesaro's niraparib NOVA study, but with some slight differences including enrollment criteria (NOVA excluded patients with residual disease >2 cm), PFS endpoint (NOVA included symptom progression with rising CA-125 as an event) and scan frequency (less frequent scans for SOLO-2). SOLO-2 utilized the new tablet formulation of olaparib that has increased bioavailability relative to approved Lynparza. Study populations appeared to be consistent between SOLO-2 and NOVA.

At the primary PFS endpoint, olaparib provided a +13.6-month PFS benefit over placebo via investigator assessment, which translated to a 70% reduction in risk of progression or death (HR=0.30, p<0.0001). However, a sensitivity analysis using blinded central review demonstrated a +24.7-month PFS benefit over placebo (HR=0.25, p<0.0001). This difference could be driven by scan frequency, when progression is officially called, and/or how the data was processed. Regardless, at worst we believe olaparib performed in-line with niraparib which provided a +15.5-month PFS benefit over placebo in gBRCA+ patients in NOVA, a 73% reduction in risk of progression or death (HR=0.27, p<0.0001). The placebo arms between the two studies performed nearly identically, both having a mPFS of 5.5 months.

Several secondary endpoints were either in-line or slightly favored olaparib over niraparib including time to first subsequent therapy (TTFST), PFS2 and time to second subsequent therapy. TTFST is worth noting as we believe it cannot be confounded by scan frequency and study progression criteria; mTTFST slightly favored olaparib over niraparib. Olaparib produced a +20.8-month benefit over placebo at mTTFST (HR=0.28) vs. +12.6-month benefit for niraparib over placebo (HR=0.31).

In terms of safety, olaparib showed a more tolerable safety profile than niraparib. High-grade GI toxicity was similar between olaparib and niraparib (nausea: 2.6% vs. 3.0%, vomiting: 2.6% vs. 1.9%, diarrhea: 1.0% vs. 0.3%), but high-grade heme AEs were significantly lower with olaparib. Grade 3/4 thrombocytopenia, anemia and neutropenia for olaparib and niraparib were 1.0% vs. 33.8%, 19.5% vs. 25.3%, and 5.1% vs. 19.6%, respectively. All this translated to fewer dose reductions and discontinuations in the olaparib arm of SOLO-2 than the niraparib arm of NOVA. AEs leading to dose reduction occurred in 25.1% of patients in SOLO-2 compared to 66.5% of patients in NOVA. Discontinuations due to AE were reported to be 10.8% in SOLO-2 vs. 14.7% in NOVA.

Olaparib vs. Niraparib Safety Comparison

	NOVA	SOLO-2
	Niraparib (n=367)	Olaparib (n=196)
Most common grade 3/4 AEs		
Thrombocytopenia	33.8%	1.0%
Anemia	25.3%	19.5%
Neutropenia	19.6%	5.1%
Fatigue	8.2%	4.1%
Hypertension	8.2%	-
Nausea	3.0%	2.6%
Vomiting	1.9%	2.6%
Diarrhea	0.3%	1.0%
Treatment interruptions	68.9%	-
Dose reductions	66.5%	25.1%
Treatment discontinuations	14.7%	10.8%

Source: Company data

KOLs have consistently said that PARPs would be viewed interchangeably from the efficacy perspective. Thus, safety will likely be a critical competitive advantage, especially in the maintenance setting.

Confirmatory SOLO-3 Hits ORR And PFS, Largely Expected

In December 2018, AZN announced that Lynparza hit ORR (primary endpoint) and PFS (key secondary endpoint) in the pivotal Phase III SOLO-3 trial (n=266). SOLO-3 is a confirmatory trial that was initiated in February 2015, after Lynparza's accelerated approval in 2014. The trial is evaluating Lynparza in 3L-5L BRCA-mutated relapsed ovarian cancer and had a primary completion in October 2018. The data were presented at ASCO'19. ORR was 72% for Lynparza vs. 51% for chemo (OR 2.35; 95% CI 1.40–4.58; P=0.002) and PFS HR was 0.62 (95% CI 0.43–0.91; P=0.013; median 13.4 vs. 9.2 months). No new safety signals appeared. Based on the outcomes of previous datasets, positive readouts for SOLO-3 were largely expected.

Study 19 Also Supported Maintenance Approval

Lynparza's broad label was supported by Study 19, which used the older capsule formulation. The Phase II Study 19 trial was updated at ASCO 2016. This study enrolled a patient population similar to NOVA and included 265 patients with platinum-sensitive recurrent high-grade serious ovarian cancer. Patients were required to have received at least 2 prior rounds of platinum chemotherapy and achieve a CR or PR to their most recent platinum-based chemotherapy regimen with no evidence of progression. Patients were then randomized 1:1 to receive olaparib or placebo until progression or unacceptable toxicity. In the ITT population (included patients with wildtype BRCA), the study reported a statistically significant 3.6-month improvement for the olaparib arm in mPFS (4.8 vs. 8.4 months; HR=0.35, p<0.001). In the BRCA+ cohort (germline or somatic mutation), the median PFS was 4.3 and 11.2 months for placebo and olaparib (+6.9-month benefit; HR=0.18, p<0.0001), respectively. In the non-BRCA+ cohort, median PFS was 5.5 months for placebo and 7.4 months for olaparib (HR=0.54, p=0.0075). At the 3rd OS analysis, olaparib continued to show an OS benefit in the ITT but failed to clear the high statistical hurdle (p<0.0095). Median OS was 27.8 months for placebo and 29.8 months for olaparib (HR=0.73, p=0.02483). In line with PFS analyses, the OS benefit provided by olaparib was more robust in the mBRCA+ cohort. Median OS for this group was 30.2 months for placebo and 34.9 months for olaparib (HR=0.62, p=0.0248). The

exploratory endpoint of time to first subsequent therapy also demonstrated olaparib superiority over placebo in both the BRCA mutant and wildtype cohorts.

Solid Data In BRCAm Breast Cancer

Full Phase III data in 2L HER2- germline BRCA1/BRCA2 breast cancer (OlympiAD; n=302) was presented at ASCO:17 showing statistically significant and clinically meaningful improvement in PFS (primary endpoint) of 7 months for Lynparza patients vs. 4.2 months for chemo arm. The response rate was 60% for Lynparza vs. 29% for chemo. ORR and PFS are slightly ahead of that presented by competitors, but the OlympiAD population was less pretreated. There was a lower incidence of grade 3+ AEs on Lynparza vs. chemo (36.6% vs. 50.5%), and fewer discontinuations (4.9% vs. 7.7%).

The data is solid and in line with our mPFS expectations. The discussant observed that the comparison arm represented older therapy, and therefore may have provided an easy comparison. On the other hand, it may have provided a higher hurdle for toxicity.

In April 2018, final OS data was presented showing a Lynparza mOS of 19.3 months vs. 17.1 months for chemotherapy. The trial was not powered for OS. At the final OS data cut-off (64% maturity), 13% of patients remained on Lynparza and no patients on chemo.

Phase III PROfound Top Line Positive; mCRPC Filing Expected In 2020

In August 2019, AZN announced that Phase III PROfound met its primary endpoint of rPFS improvement. PROfound (n=245) tested Lynparza vs. enazalutamide or abiraterone in late-line mCPRC patients with HRR mutations. Fifteen predefined genes were used to determine HRR alteration, of which BRCA1/2 and ATM were grouped into Cohort A with 12 other HRR alterations (BRIP1, BARD1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D or RAD54L) comprising Cohort B. The primary endpoint was rPFS in Cohort A with secondary endpoints including rPFS in the combined cohorts, ORR, and OS. All patients had progressed on at least one novel anti-androgen and 65% of patients in Cohort A were post-chemo. Median rPFS in Cohort A was 7.39 months vs. 3.55 months for control (HR [95% CI] 0.34 [0.25-0.47], p< 0.0001), a significant improvement. 12-month PFS rate was 28.11% vs. 9.40%. ORR in Cohort A was 33.3% for Lynparza vs. 2.3% for control. In the combined cohorts, rPFS was 5.82 vs. 3.52 months (HR [95% CI] 0.49 [0.38-0.63], p< 0.0001) with 12-month PFS rate at 22.13% vs. 13.47%. Although not yet significant, mOS in Cohort A at interim was 18.50 months for Lynparza vs. 15.11 months for control (HR [95% CI] 0.64 [0.43-0.97], p=0.0173). In the combined cohorts mOS was 17.51 vs. 14.26 months (HR [95% CI] 0.67 [0.49-0.93]). In the control arm, 80.6% of Cohort A and 84.6% of Cohort B crossed over to Lynparza. Most common AEs were anaemia (46.1% vs. 15.4%), nausea (41.4% vs. 19.2%), decreased appetite (30.1% vs. 17.7%) and fatigue (26.2% vs. 20.8%) for Lynparza vs. control; 16.4% and 8.5% of patients, respectively, discontinued due to AE.

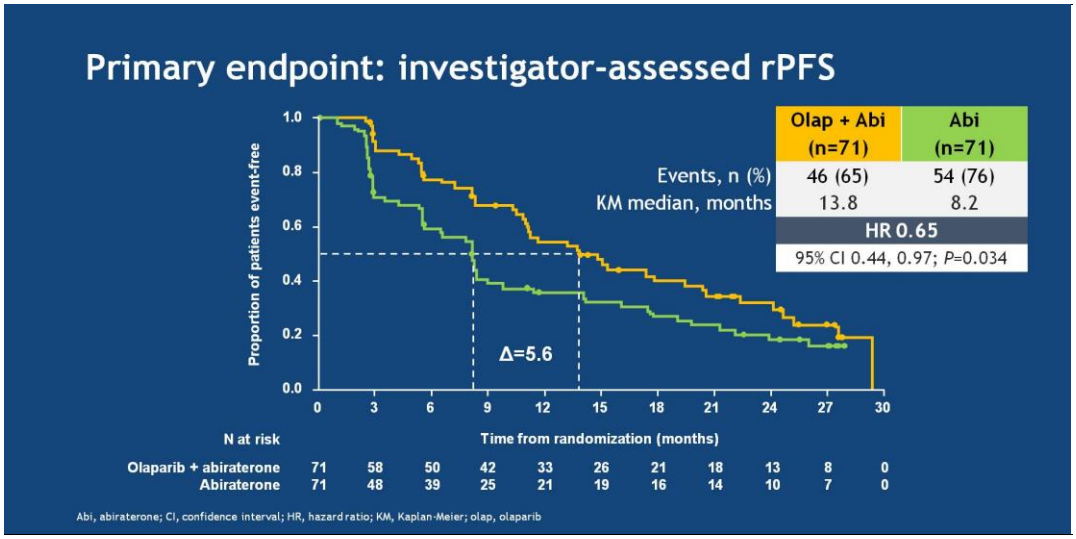
Although HRR-altered mCRPC represents a relatively small patient population, Lynparza should benefit from first mover advantage in another tumor type and maintain its lead amongst PARP inhibitors. Our KOLs were looking for median rPFS in the range of 6-8 months, an expectation that Lynparza comfortably met in Cohort A and nearly met in the combined cohorts. Prior to seeing the PROfound data, about a third of specialists surveyed by Cowen during its 22nd Annual Therapeutics Conference in September 2019 believed that 11-20% of their mCRPC patients would receive a PARP inhibitor in 2-3 years. This number is likely capped somewhere below 30%, the proportion of mCRPC patients believed to harbor mutations in DNA damage repair genes. Although likely an underestimate, it is notable that 4425 patients were screened to enroll 245 BRCA1/2 or ATM-mutant patients in Cohort A and 142 patients in Cohort B, implying incidence rates

of only 5.5% and 3.2%, respectively. It is unclear whether these data will be sufficient to earn Lynparza a label in all HRR-mutant patients or just the BRCA1/2 and ATM subgroup. Regardless, impressive rPFS and ORR results mean Lynparza is likely to be first-in-class in mCRPC where competition is not expected until 2022 (Zejula (GSK), The Phase III PROpel trial (n=720) evaluating Lynparza+abiraterone vs. abiraterone-alone in Stage IV advanced, castration-resistant prostate cancer initiated in October 2018; primary completion is April 2021.

Phase III trials were initiated based on positive interim data from the Phase II Study 08 trial (n=159) which was presented at ASCO'18 and published in Lancet Oncology in June 2018. The study evaluates Lynparza+abiraterone vs. abiraterone-alone for treatment of 2L-4L metastatic castration-resistant prostate cancer (mCRPC). Abiraterone inhibits the cytochrome p450 complex 17 alpha-hydroxylase/C17,20-lyase (CYP17), involved in testosterone production in the adrenals and testes. The Lynparza+abiraterone combo hit the primary endpoint for radiologic progression-free survival (rPFS), with a median rPFS of 13.8 months for the combination vs. 8.2 months on abiraterone-alone (HR=0.65; 95% CI: 0.44-0.97, p=0.034). Secondary outcomes for second progression or death (PFS2) and OS were also encouraging. Median PFS2 for the combo was 23.3 months vs. 18.5 months on abiraterone (HR=0.79; 95% CI: 0.51–1.21). Median OS for the combo was 22.7 months vs. 20.9 months on abiraterone (HR=0.91; 95% CI: 0.60–1.38).

A separate Phase II trial of Lynparza monotherapy in late-stage mCRPC patients (TOPARP-B) was presented at ASCO'19. One of two Lynparza doses (300 or 400mg) was administered to 3L+ mCRPC patients with DNA damage repair (DDR) defects (n=92) including BRCA1/2 mutations as well as alterations in other homologous repair genes. ORR (primary) by PSA response (>50% reduction), radiological response, or CTC count conversion as well as PFS and safety were assessed. All patients were post-ADT, 99% were post-docetaxel, 90% post-abiraterone/enzalutamide, and 38% post cabazitaxel. Overall ORR was 54% (95%CI 39-69%, meeting the primary endpoint threshold) in the 400mg cohort and 37% (95%CI 23-53%) in the 300mg cohort. Overall mPFS was 5.4 months. Of the DDR subgroups, the best responses were obtained in BRCA1/2m tumors (ORR 24/20, mPFS 8.1 months).

Lynparza+abiraterone Improves rPFS In mCRPC



Source: AZN presentation, ASCO 2018

PFS Improvement Enough For A Pancreatic Cancer Approval After A Positive AdComm

Lynparza was FDA approved for 1L maintenance treatment of germline BRCA-mutated metastatic pancreatic cancer in December 2019 after an FDA AdCom voted 7-5 in favor of Lynparza's benefit/risk. Approval was based on Phase III POLO, presented at ASCO'19. POLO(n=151) was a randomized, double-blind, placebo-controlled trial of patients with gBRCAm pancreatic adenocarcinoma not progressed on platinum-based chemo. PFS for Lynparza compared to placebo was improved, reducing the risk of disease progression or death by 47% (HR 0.53 [95% CI 0.35-0.82], p=0.004). mPFS was 7.4 months for Lynparza compared to 3.8 months for those on placebo, with more than twice as many patients remaining progression free at both one year (34% on Lynparza vs. 15% on placebo) and two years (22% vs. 10%), respectively. OS was not mature but at interim analysis was not improved. Safety was consistent with the known profile for Lynparza. This is a tough-to-treat tumor and although the PFS benefit is impressive, it did not translate to an OS improvement which significantly dampened clinician enthusiasm. Furthermore, it was suggested that chemotherapy could be continued longer than the comparator arm in the trial. Still, this is the first Phase III trial to validate a biomarker-driven treatment for pancreatic cancer and Lynparza will likely be approved in gBRCAm pancreatic cancer patients (~5-7% of PC).

Lynparza Being Evaluated In Combo With Other Drugs

Olaparib + durvalumab: Olaparib is also being evaluated in combination with durvalumab. In 2016, AZN initiated a Phase I/II study (MEDIOLA) in a basket of solid tumors including ovarian, breast cancer, SCLC, and gastric cancer, with other tumors potentially added. MEDIOLA data in ovarian cancer was presented at SGO in March 2018, in which Lynparza showed an ORR of 72% in the full cohort, but 77% in patients who had one prior therapy. Given that DDR deficient tumors have high mutational burden, AZN expects a strong additive effect and potential synergy from this combo. The estimated primary completion for MEDIOLA is in August 2022.

Lynparza+Imfinzi is also being studied in the Phase II BAYOU study for Stage IV 1L cis-platinum chemotherapy-ineligible urothelial bladder cancer. The trial initiated in March 2018, intends to enroll 256 patients, and has a primary completion date for February 2020 on a PFS endpoint. In addition, in H1:2018 AZN announced plans for a Phase III DUO-O trial (n=1,056) for Lynparza+Imfinzi in Stage IV 1L ovarian cancer. DUO-O initiated in January 2019 and has a primary completion for May 2022 assessing a PFS primary endpoint.

Olaparib + capivasertib (AKT inhibitor): At AACR'16, Astra presented early Phase I ComPAKT trial data for capivasertib (AZD5363; AKT inhibitor) + Lynparza in solid tumors. The combination had a manageable toxicity with one DLT and most common grade 3 toxicities being anemia (7-13%), rash (4-7%), vomiting, diarrhea and proteinuria. Of the 37 patients evaluable for efficacy, 10 experienced a response and included patients with ovarian, breast or prostate cancer with or without BRCA mutation. The data suggests Lynparza may be found clinically relevant beyond ovarian BRCAm cancer when combined with AKT inhibition. Separately, in June 2019, capivasertib+chemo advanced into Phase III for metastatic TNBC.

Tagrisso Dominates In 1L And 2L EGFR+ NSCLC On Impressive Data

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Tagrisso (osimertinib/AZD9291) is a third-generation oral irreversible EGFR inhibitor that targets both activating sensitizing EGFRm and the resistance mutation T790M in NSCLC. It is approved in both 1L and 2L EGFRm positive NSCLC which occurs in 10-15% of all NSCLC in Western countries and in about 30-40% in Asia. Testing rates for the EGFR mutation have increased in the U.S. and EU, with the U.S. rate at approximately

80%. Tagrisso was approved in China in March 2017. The company estimates that China could be as large as the U.S. market given high prevalence (Astra estimates that 30-40% of NSCLC patients in China have the EGFR mutation) and large population.

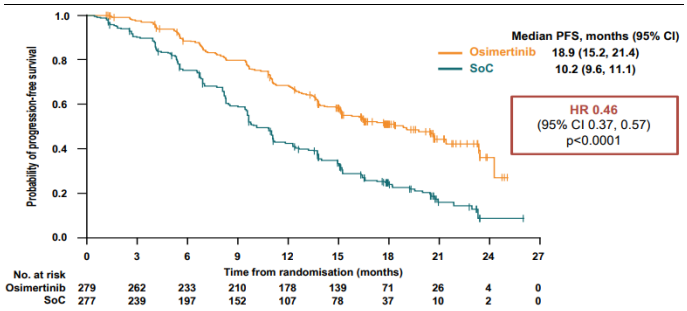
Tagrisso's label was expanded to include 1L EGFRm NSCLC in April 2018 in the U.S., June 2018 in the EU, August 2018 in Japan, and September 2019 in China. Astra estimates the U.S. 1L new patient share at 80% as of Q3:19. Approval in the 1L setting was based on Phase III FLAURA. Phase III trials are ongoing in Stage III unresectable NSCLC post chemoradiation (LAURA, n=200, primary completion October 2021, primary endpoint PFS) and in the adjuvant NSCLC setting (ADAURA, n=700, primary completion Feb 2022, primary outcome is DFS).

Astra estimates potential Tagrisso sales of $4B, which includes first-line, but could be greater if successful in the adjuvant setting. We estimate Tagrisso sales of $3.245B (+74%) in 2019, $4.51B in 2020, and $8.65B in 2025.

FLAURA Data Usher Tagrisso In As Leader In 1L EGFR+ NSCLC

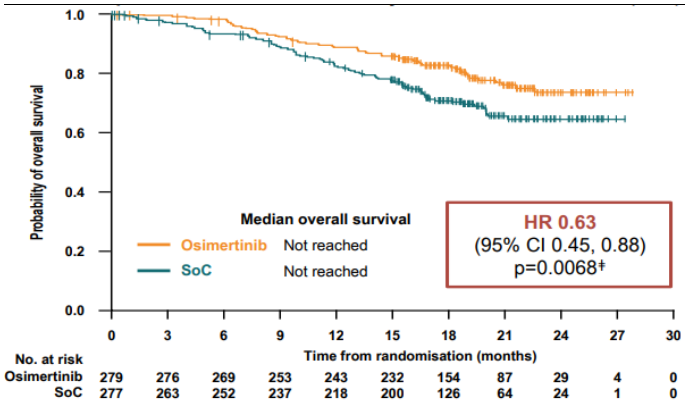
Full data from the Phase III FLAURA trial were presented at ESMO:17 (Sept). Median PFS was 18.9 months for patients on osimertinib vs. 10.2 months for the comparator arm (previous SOC treatments gefitinib and erlotinib). In January 2018, Phase III FLAURA results were published in the NEJM, in which Tagrisso demonstrated a significantly improved primary endpoint mPFS (18.9 months) vs. standard EGFR-TKIs (10.2 months; HR=0.46, 95% CI: 0.37- 0.57, p<0.001). ORR was similar for Tagrisso (80%) vs. other EGFR-TKIs (76%; odds ratio = 1.27). OS data (secondary endpoint) were still immature, however, 18-month survival was 83% on Tagrisso (95% CI: 78-87%) vs. 71% with standard EGFR-TKIs (95% CI: 65-76; HR=0.63, p = 0.007). An additional update was presented at ASCO'18, in which patients receiving 1L Tagrisso had significantly improved median time to first subsequent therapy or death (23.5 months) vs. standard EGFR-TKIs (13.8 months; HR=0.51, p < 0.0001). Final OS data were presented at ESMO 2019 showing HR 0.799 (95% CI 0.641-0.997, p=0.0462) and mOS 38.6 vs. 31.8 months. In October 2018 at ESMO, AZN presented the mechanisms of acquired resistance to 1L Tagrisso in Phase III FLAURA to be MET-amplification (15%), then EGFR C797S mutation (7%), followed by HER2-amplification, PIK3CA mutation, and RAS mutation (2-7%). In the comparator TKI-arm (erlotinib or gefitinib), the most frequent mechanism of acquired resistance was the EGFR T790M mutation (47%).

FLAURA PFS Data



Source: AstraZeneca ESMO 2017

FLAURA OS Interim Data



The Tagrisso data are superior to Iressa/Tarceva on PFS. Our KOLs will use it as the 1st line standard in EGFR mutants given tremendous PFS benefit, better tolerability, and probable OS benefit. The data reflect the properties of the molecule: 1) better BBB penetrability than current SOC and 2) activity vs. T790M (mutation driving primary resistance to first gen TKI) making it a first-choice EGFR inhibitor.

The totality of the data suggests Tagrisso is superior to standard EGFR-TKIs in 1L treatment of EGFR+ NSCLC. In-line with the FLAURA trial, surveyed specialists believe the typical front-line patient will be treated with Tagrisso for ~20 months. At our annual Therapeutics Conference in 2018, our panelists noted that the typical patient will be treated with Tagrisso for just over 18 months prior to progression (as defined by RECIST criteria), with treatment continuing for an additional month or two as progression is confirmed and alternative therapies are discussed.

Continued Evaluation Of Osimertinib Resistance

In October 2018 at ESMO, AZN presented new data on the mechanisms of acquired resistance from osimertinib in front-line treatment (from Phase III FLAURA) and in second-line treatment (from Phase III AURA3). In 91/279 osimertinib-treated patients who progressed or discontinued in front line, the most frequent acquired resistance mechanisms were MET-amplification (15%) and EGFR C797S mutation (7%), followed by HER2-amplification, PIK3CA, and RAS mutations (2-7%). In 83/279 osimertinib-treated patients who progressed or discontinued in second-line, the most frequent mutations detected were EGFR C797 mutations (15%; C797S n=10; C797G n=1), MET-amplification (19%), HER2-amplification (5%), and PIK3CA mutation (5%). Based on these results, there are a number of Phase II trials underway testing osimertinib in combination with agents that target these pathways (MEK inhibitor selumetinib or MET inhibitor savolitinib, Ph II TATTON and SAVANNAH, PC March 2020 and August 2021).

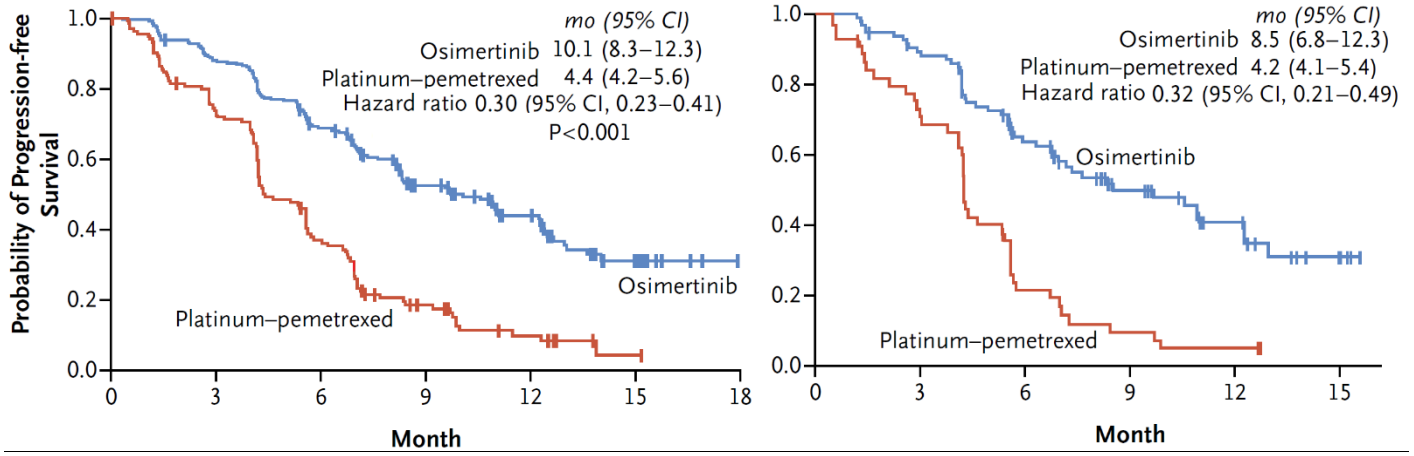
Osimertinib In Adjuvant Setting

In 2015, AstraZeneca initiated the pivotal ADAURA trial to evaluate osimertinib in the adjuvant setting. Here, ~700 patients eligible for surgical resection will be randomized following surgery to receive either osimertinib or placebo. Those enrolled into the study will be required to have mutant EGFR (exon 19 deletion or L858R) ± T790M mutation. The primary endpoint of the study is disease free survival. Top-line data from this trial are anticipated in 2022.

Strong Data Supported Approval In 2L Setting

Tagrisso's approval in 2L EGFR+ NSCLC is based on Phase I/II AURA and AURA2, which showed response rate of 57-61% in EGFR T790M mutation positive NSCLC who had progressed on prior TKIs (Tarceva, Iressa, Gilotrif). T790M is found in ~50-60% of patients resistant to first generation TKI. The response rate is impressive given prior standard of care (afatinib+cetuximab) delivers responses ~25%. Similar to other EGFR inhibitors, the most common adverse events included GI and derm toxicities (diarrhea, rash). In confirmatory Phase III study (AURA3), Tagrisso reduced the risk of death or progression by 70% vs. platinum-based chemotherapy (mPFS 10 months vs. 4.4 months, HR=0.30, p<0.001). Importantly, among patients with CNS involvement, Tagrisso delivered 8.5 months of mPFS vs. 4.2 months for chemotherapy. In March 2017, Tagrisso was granted regular U.S. approval (from accelerated) based on the AURA3 data; full EU approval was received in April 2017.

AURA3: Tagrisso Reduced The Risk Of Death Or Progression In T790M+ NSCLC In Both The ITT (Left) And In Patients With CNS Involvement (Right)



Source: Company data

Iressa Declining As Focus Shifts To Tagrisso

Iressa (gefitinib) is a tyrosine kinase inhibitor that targets EGFR activating mutations (exon 19 deletion or exon 21-point mutation L858R) involved in cell growth and proliferation in NSCLC. EGFRm positive NSCLC occurs in 10-15% of all NSCLC in Western countries and in about 30-40% in Asia. The drug was first approved in the U.S. in 2004 and in the EU in 2009.

In the U.S., Iressa has negligible share as ISEL study failed to show an OS benefit while a similar study for Roche's Tarceva achieved its OS endpoint. OUS, Tarceva and Iressa split the EGFR NSCLC market as Iressa is commonly used in the Asia and Europe. The patent expired in 2019 in the EU and will expire 2022 in the U.S. Astra has shifted marketing efforts to Tagrisso. We estimate Iressa sales of $420MM (-19%) in 2019, $335MM in 2020, and $140MM in 2025.

Selumetinib Misses In Uveal Melanoma, NSCLC, And Thyroid; Under Review For Neurofibromatosis

Selumetinib (AZD6244) is a potent, selective, ATP uncompetitive inhibitor of MEK1/2, licensed from Array. In July 2015, AstraZeneca announced that selumetinib did not meet its primary endpoint (PFS) in the Phase III SUMIT trial in uveal melanoma. In July 2016, Astra announced that selumetinib did not meet its primary endpoint (PFS) in a Phase III trial (SELECT-1; n=634) in 2L KRASm NSCLC. And in July 2018, Astra announced that the primary endpoint in the Phase III ASTRA trial in differentiated thyroid cancer (DTC) was not met.

In February 2018, selumetinib received Orphan Drug Designation for use in neurofibromatosis Type 1 (NF1); EU Orphan Designation granted in August 2018. In November 2019, the NDA for selumetinib was accepted by the FDA with a PDUFA in Q2:20. Interim data for the NF1 Phase II SPRINT trial was recently presented at ASCO'18, in which selumetinib demonstrated 72% PR and 24% SD in 50 evaluable patients. In addition, selumetinib hit statistical significance for pain intensity/inference at 1-year, as well as strength and range-of-motion at 1-year. Selumetinib is also part of the Merck collaboration (discussed previously in Lynparza section). We estimate selumetinib sales of $15MM in 2020, and $300MM in 2025.

Phase II Data In Neurofibromatosis Encouraging, Under Priority Review

Phase II SPRINT data in neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN) was presented at ASCO 2018. Out of 50 children enrolled, the most frequent PN-related morbidities were disfigurement (n=44), motor dysfunction (n=33), and pain (n=28). As of November 2017, the median cycle number was 19.5, with 38 patients remaining on treatment. The median change in PN volume from baseline was -27.7%. The best response PR occurred in 72% of patients, stable disease occurred in 24% of patients, and 4% of patients had no re-staging. Of the 36 patients with PR, 32 were confirmed on 2+ consecutive re-staging scans and 22 continue to have a PR beyond 1 year. Parent and child-reported pain intensity and pain interference scores significantly improved ($p < 0.01$), as did strength (0-5 scale) and range of motion (degrees) of affected muscle groups/joints ($p < 0.01$). Selumetinib dose was reduced in 12 patients; 5 patients were removed from treatment. SPRINT primary completion is estimated to be August 2021.

With 72% of patients showing a PR, and 44% of patients showing a durable PR for 1+ years, depth and durability are impressive. This Phase II data confirms the 71% PR achieved in Phase I. Currently, there are no approved therapies for NF1. In February 2019, the FDA granted selumetinib Orphan Drug Designation for NF1, which has a prevalence of about 1/2,500 - 1/3,000 births; Breakthrough Therapy designation was granted in April 2019.

Calquence Approved For MCL And CLL

In February 2016, Astra acquired a 55% equity stake in privately held Acerta Pharmaceuticals for $4B. Astra obtained access to lead product Calquence (acalabrutinib/ACP-196), a second-generation BTK inhibitor with best-in-class potential due to: greater target selectivity, short half-life (BID dosing may enable more consistent target engagement compared to ABBV's Imbruvica, which is dosed QD), and improved tolerability (which may include lower bleeding, rash, GI toxicities and atrial fibrillation risks). Calquence does not inhibit the EGFR pathway (drugs that inhibit such signaling are associated with AEs such rash and diarrhea), the ITK pathway (a critical modulator for NK cell function), nor the TEC pathway, which is important for platelet aggregation.

In February 2016, the EMA granted acalabrutinib Orphan Drug designation for CLL/SLL, MCL (mantle cell lymphoma), and Waldenstrom's macoglobulinemia. Calquence was granted accelerated approved for 2L MCL in the U.S. in October 2017, well ahead of its January 2018 PDUFA. Astra estimates that Calquence has over one-third of 2L MCL U.S. market. The average monthly WAC price is approximately $14,259, based on the 100mg dose BID. In November 2019, Calquence was approved in the U.S. for treatment-naïve CLL.

Astra estimates potential peak sales of acalabrutinib, for all B-cell indications, to be $5B+. We estimate Calquence sales of $165MM (+166%) in 2019, $320MM in 2020, and $1,300MM in 2025.

Calquence Data Positive In CLL

Mid-2019, Calquence posted positive topline results from two Phase III CLL programs (ASCEND and ELEVATE-TN) and is building the case that it is a safer, equally efficacious option relative to Imbruvica. A Phase III head-to-head trial in 2L CLL (n=533) is ongoing and, combined with the slate of CLL data already generated, could garner significant share for Calquence.

In Q2:19, AZN reported that both Phase III ASCEND (Calquence monotherapy in r/r CLL) and ELEVATE-TN (Calquence +/- chlorambucil+obinutuzumab in treatment-naïve CLL) met their primary endpoints at interim analyses. Phase III ASCEND data were presented at EHA'19. At median 16mo follow-up, Calquence-treated r/r CLL patients showed PFS HR of 0.31 (95% CI, 0.20-0.49, p<0.0001) vs. rituximab combined with idelasib or bendamustine. In a cross-trial comparison, Calquence resulted in lower rates of bleeding relative to Imbruvica (RESONATE at 9 mo.): 26% vs. 44%. ELEVATE-TN data were presented at ASH'19. Phase III ELEVATE-TN (n=535) assessed Calquence (acalabrutinib, 100mg BID) with or without Gazyva (obinutuzumab, RHHBY) vs. Gazyva+chorambucil in treatmentnaive CLL patients ≥65 years old or <65 years old with coexisting conditions. The primary endpoint was PFS in the combination arm. PFS in the monotherapy arm, OS, and safety were key secondary endpoints. The trial met its primary endpoint - results at a median follow-up of 28 months are displayed in the table below.

Calquence vs. Imbruvica In 1L CLL

	ILLUMINATE		ELEVATE-TN		
Efficacy Endpoint	***Imbruvica+Gazyva***	***Chlorambucil+Gazyva***	***Calquence***	***Calquence+Gazyva***	***Chlorambucil+Gazyva***
mPFS	NR	19	NR	NR	22.6
PFS HR	0.23	-	0.20	0.10	-
Estimated 30mo OS			95%	94%	90%
ORR	89%	73%	85%	94%	79%
CR	20%	8%	0.6%	13%	5%
PR	69%	66%			
Grade 3+ AE					
Discontinuation	16%		9%	11%	14%
Diarrhea	3%	0%	1%	1%	0%
Rash	3%	0%			
Pneumonia	9%	4%	0%	6%	2%
Hypertension	4%	3%	2%	3%	3%
Atrial Fibrillation (any grade)	12%	0%	4%	3%	1%
Neutropenia	39%	48%	9%	30%	41%
Thrombocytopenia	19%	11%	3%	8%	12%
Anemia	4%	8%	7%	6%	7%

Source: Product labels; Cowen and Company

Improved safety with as good or better efficacy makes Calquence a real challenger to Imbruvica (ABBV/JNJ) in 1L CLL. Calquence is a more selective covalent BTK inhibitor, possibly accounting for its improved CV safety profile. Calquence was approved for MCL in 2017 but these data will give the drug access to the larger CLL market. The FDA granted Breakthrough Therapy Designation for this indication in August 2019. This trial does not compare directly to Imbruvica but cross-trial differences in atrial fibrillation rates could convince physicians to reconsider their therapy of choice, especially in at-risk patients. Calquence could also capture switch patients who poorly tolerate Imbruvica. For its part, Imbruvica has long-term efficacy data and commercial momentum that cannot be matched by new entrants, and we think it will remain the leader in CLL. These Calquence trials were supported by positive early stage data in ACE-CL-001, ACE-CL-208, and ACE-CL-003.

At ASH:16, data from the Phase I/II ACE-CL-001 trial showed that acalabrutinib delivered a response rate of 79% in Imbruvica-intolerant patients with CLL/SLL. However, two cases of treatment-emergent atrial fibrillation occurred (out of 33 patients). One event was grade 2 in nature and was experienced by a patient who discontinued flecainide (antiarrhythmic agent). No recurrence was observed when

flecainide was restarted. The second event was grade 3 in nature and was experienced by a patient with pleural effusion and pseudomonal infection. The event resolved after 2 days.

An update for the Phase I/II ACE-CL-001 trial was provided at ASH'17 and published in the Blood Journal in December 2017. A total 134 patients received treatment, including 132 with CLL and 2 with Small Cell Lymphocytic Lymphoma (SLL). On a median follow-up of 19.8 months, ORR was 85% (2% achieving CR). Median time to response was 4.7 months, 18-month DOR rate was 85% (mDOR not reached), and 18-month PFS was 88% (mPFS not reached). The most common AEs of any grade were headache (46%), diarrhea (43%), upper respiratory tract infection (28%), fatigue (27%), nausea (27%). Grade 3+ AEs were said to be infrequent, consisting mostly of neutropenia (11%) and pneumonia (10%). Notably, 3% of patients experienced afib of any grade (2% were grade 3+).

Data from Phase I/II ACE-CL-208 (Calquence mono in Imbruvica-intolerant r/r CLL) and ACE-CL-003 (Calquence+obinutuzumab in TN and r/r CLL) were presented at ASCO'19. ACE-CL-208 provided compelling evidence that Calquence is a safer option than Imbruvica. About 10% of CLL patients are thought to be intolerant to Imbruvica, and as many as 40-50% of elderly patients. In this trial, patients that could not tolerate Imbruvica were treated with Calquence monotherapy and discontinuation due to AEs occurred in only 17%. In ACE-CL-003, treatment-naïve (n=19) and r/r CLL (n=26) patients were treated with Calquence+obinutuzumab and assessed for ORR (primary), PFS, minimal residual disease (MRD), and safety. Median age was 61. ORR was 95% and 92% (CR = 32% and 8%) in 1L and 2L+, respectively. mPFS was not reached for either group but 36-month PFS was 94% and 73%.

MCL Data Shows Solid Efficacy And Reasonable Safety

The FDA granted accelerated approval of Calquence for adults with previously treated MCL in October 2017, based on the Phase II ACE-LY-004 study. Safety and efficacy data from the trial were presented at the 60th annual ASH Meeting in December 2017. From 124 patients with a median of 2 prior therapies, investigator-assessed ORR was 81% (40% CR, 41% PR). Median duration of response, PFS, and OS had not been reached within the period of assessment (as of Feb 28, 2017). The 12-month DOR was 72%, PFS was 67%, and OS 87%. Grade 3-4 AEs included neutropenia (10%), anemia (9%) and pneumonia (5%). There were no cases of atrial fibrillation, 1 case of Grade 3 hypertension, and all bleeding events were Grade 1/2 except 1 case of Grade 3 GI hemorrhage in a patient with history of a GI ulcer.

At ASH 2018, AZN presented a long-term follow-up of Calquence monotherapy in Phase II ACE-LY-004. With a median follow-up of 26.3 months, 40% of patients remain on treatment. Investigator-assessed ORR was 81% (consistent across prespecified subgroups), 43% of patients achieved CR, and median DOR was 25.7 months. Median PFS was 19.5 months. While median OS was not reached, the 24-month OS rate was estimated to be 72%.

Calquence Could Offer Advantages Over Competition In MCL

ABBV's Imbruvica is a BTK inhibitor, but also acts as an interleukin-2-inducible kinase (ITK) inhibitor. In MCL, there has been considerably more data from Imbruvica (8 of 13 studies Phase I-III; including combinations), and for longer durations (out to 5 years). Data presented at ASH 2017 combines 4 studies (n=370) for overall mPFS of 13 months, mOS of 26.7 months, and ORR of 70% (27% CR, 43% PR, 12% SD). ORR for patients who had received 1 prior line of therapy was about 78%, while ORR for patients receiving >1 line was about 67%.

In comparison, Calquence is a more selective BTKi, with potentially less off-target effects. Despite having accelerated approval in MCL, the only data we have seen thus far is interim from the Phase 2 ACE-LY-004 trial, presented at ASH'17 (data above).

Regarding safety, treatment with Imbruvica elicited grade ≥3 AEs for atrial fibrillation (in 6-9% of patients), bleeding (up to 6%), anemia (9%), neutropenia (11%), and pneumonia (5%). Calquence had only slightly lower rates for anemia (7%), neutropenia (9%), and pneumonia (4%). However, Calquence had no cases of atrial fibrillation, and only 3 cases of grade ≥3 cardiac AEs. Calquence bleeding events occurred in 31% of patients and were all grade 1 or 2, except for one grade 3 GI hemorrhage in a patient with a history of GI ulcer. Notably, Calquence has a drug-drug interaction with PPIs.

Calquence results in MCL are impressive (reflecting the FDA's early nod), however, longer/larger studies are needed to confirm both efficacy equivalence and safety superiority. Newer BTK inhibitors like Calquence have improved specificity of mechanism, which typically decreases toxicity. Sometimes more selective agents are less effective – this has not been seen after 12 months on Calquence, but longer durations are needed. If confirmed, acalabrutinib could pose a threat to Imbruvica. Timeline is uncertain, but it appears KOLs look for at least 1 more year of Calquence data. Durability of response is important. It is possible that Calquence's higher CRs could lead to greater durability of response, although this is dependent on the relative length of follow-up in each data set. The depth of response in BTK studies can improve for many patients with longer follow-up. MCL represents 3-6% of new NHL cases per year in western countries.

Impressive 2-Year Data For Calquence In Waldenstrom Macroglobulinemia, May Be Tempered By Safety Concern

Data from a Phase II study in Waldenstrom Macroglobulinemia (WM) was presented at ASCO 2018. ORR was 93% in TN and RR patients; median DOR and OS was not reached after 2 years of follow-up. Two-year PFS was 90% and 82% in TN and RR patients. There were 5 cases of afib, but only one was grade 3. After Mantle Cell Lymphoma, WM is the next potential indication for Calquence. The WM data appear solid and suggests that Calquence has impressive single agent activity. However, the five cases of afib – confirming a signal picked up previously - may suggest that acalabrutinib's higher selectivity for BTK and reduced potency for TEC, EGFR, ITK may not be sufficient to spare some of Imbruvica's side effects.

Partnership Adds Promising Breast Cancer Agent Enhertu (Trastuzumab Deruxtecan)

In March 2019, Astra established a partnership with Daiichi Sankyo for Enhertu (trastuzumab deruxtecan/DS-8201), a HER2-targeted antibody-drug conjugate with a potent topoisomerase I inhibitor payload in late stage clinicals for breast cancer. Other HER2+ tumors will be explored including gastric and NSCLC. Our KOLs anticipate use in many patients with metastatic HER2+ disease. Low HER2+ shows promise but requires more data. Toxicity, particularly pulmonary, could be a limitation, particularly in early stage disease. However, AZN notes that safety protocols potentially could temper this risk. Initial filing in advanced/refractory breast cancer was completed in Q3:19 and Priority Review was granted by the FDA in October 2019. Early approval was granted in December 2019. Partner Daiichi Sankyo filed the drug in Japan in September 2019. We estimate revenue from the Enhertu collaboration to be $65MM in 2020 and $585MM in 2025.

Astra will pay Daiichi $1.35B upfront (half was paid at March 29th closing, half will be paid 12 months later) plus contingent payments of up to $5.55B ($3.8B for regulatory milestones, $1.75B for sales milestones). The companies will equally share develop/commercialization costs and profits worldwide, except in Japan where Daiichi will retain rights. Daiichi will record sales in the U.S. and certain EU markets; Astra will record its profit share in these markets in Collaboration Revenue and will record sales in all other markets (estimated to be about one-third of total sales ex-Japan) with profits to Daiichi recorded in COGS. The transaction is expected to be neutral to core EPS in 2019, with growing accretion starting 2020 and a "significant contribution" in 2023.

The current development plan for trastuzumab deruxtecan is to demonstrate efficacy in HER2+ breast cancer post-HER2 therapy including Herceptin and Kadcyla. The rationale is that the potent payload, high drug to antibody ratio, and cleavable linker on the molecule will combine to confer sensitivity to otherwise resistant tumors. Promising Phase I data have already been generated demonstrating efficacy in the third-line in patients that progressed on Kadcyla; ORR was 59.5%. It was subsequently announced in May 2019 that the analogous Phase II DESTINY-Breast01 met its primary endpoint of ORR. Phase II DESTINY-BREAST01 tested DS-8201 (trastuzumab derxutecan, 5.4mg/kg) in HER2+ breast cancer patients that had progressed on 2+ prior HER2-targeted therapies (all Kadcyla and Herceptin-experienced, median 6 prior lines). Of n=184 evaluable patients, ORR was 60.9% (up slightly from 59.5% in Ph I) including 6% CRs. Median DoR was 14.8 months, mPFS was 16.4 months, and estimated 12-month OS was 86%. Grade 3+ neutropenia (20.7%), anemia (8.7%), nausea (7.6%), decreased white cell count (6.5%), decreased lymphocyte count (6.5%), and fatigue (6.0%) were the most common high-grade AEs. Interstitial lung disease (ILD) occurred in 13.6% of patients, including 4 deaths (2.2%). These data will be used to file. Ongoing and future trials will examine trastuzumab deruxtecan in 2L (vs. Kadcyla) and in HER2-low breast cancer post-CDK4/6 inhibition.

Cardiovascular/Metabolic

Brilinta Continues Strong Growth, Trials Show No Benefit vs. Aspirin/Plavix In Stroke/PAD

Brilinta/Brilique (ticagrelor) is a twice-a-day antiplatelet that targets the $P2Y_{12}$ ADP-receptor. Brilinta was designed to have a more rapid onset and more pronounced platelet inhibition than Plavix. Brilinta was approved in the U.S. in 2011 and in the EU in 2010. The drug is indicated to reduce the risk of CV death, MI and stroke in patients with acute coronary syndrome (PLATO) or a history of myocardial infarction (PEGASUS). In both studies, the drug reduced the risk of experiencing CV events by ~15% but also showed an increased risk of bleeding when used as add-on to aspirin.

In September 2015, the FDA approved Brilinta for expanded long-term use in patients with a prior-MI based on results from the PEGASUS TIMI-54 study at a 60 mg dose. In 2016, Astra announced that Brilinta was no better than aspirin in preventing CV events in patients with a history of stroke (SOCRATES) and no better than generic Plavix in patients with peripheral artery disease (EUCLID). Brilinta was filed in H2:19 for use in high-risk T2DM/CAD patients (THEMIS-PCI). AZN is pursuing Brilinta in sickle cell anemia (Ph II HESTIA2), as well as ischemic stroke in the Phase III THALES trial (data readout expected in 2020) after the failure of the Phase III SOCRATES study. In 2016, AZN suspended programs in peripheral artery disease (PAD). A second trial in stroke patients (THALES) was recently initiated with data readout expected in 2020. The U.S. and EU patent expiration is 2024. We estimate worldwide Brilinta sales of $1.59B (+20%) in 2019, $1.675B in 2020, and $1.49B in 2025.

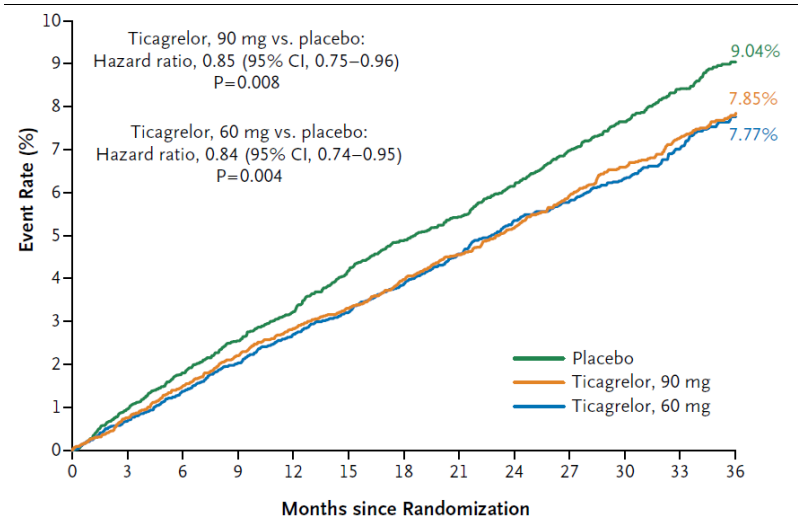
Brilinta Shows Solid Data In Patients With Prior Acute Coronary Syndrome (PLATO)

In PLATO (n=18,624), Brilinta reduced the one-year risk of CV death, MI or stroke by 14% vs. Plavix (9.8% vs. 11.7%, HR=0.84, p<0.001) in patients admitted to the hospital with an acute coronary syndrome. The study also showed a statistically significant reduction in mortality (5.8% for Brilinta vs. 6.9% for Plavix, p=0.005). Importantly, no significant difference in the rates of major bleeding was observed between Brilinta and Plavix (11.6% vs. 11.2%; p=0.22). However, Brilinta was associated with more episodes of intracranial bleeds (26/9333 vs. 14/9291) and fatal intracranial bleeds (11/9333 vs. 1/9291) but fewer episodes of other types of fatal bleeds (9/9333 vs. 21/9291). Editorial of the NEJM notes that the study is positive as the reduction in CV events was not associated with an increased risk of bleeding. However, it also notes that the incremental benefit offered by Brilinta appears on par with Effient (LLY).

Brilinta Shows Solid Data As Add-On To Aspirin In Patients With Prior MI (PEGASUS)

In PEGASUS (n=21,162), Brilinta as add-on to aspirin reduced the three-year risk of CV death, MI or stroke by 14-15% (7.7-7.8% vs. 9.0%, HR=0.84-0.85, p=0.004-0.008) in patients with prior myocardial infarction. Both doses of Brilinta (60-90 mg) showed a statistically significant reduction in major CV thrombotic events. Kaplan-Meier rates at 3 years were 7.85% in the group that received 90 mg Brilinta twice a day, 7.77% in the groups that received 60 mg of Brilinta twice daily and 9.04% in the placebo group.

PEGASUS-TIMI54: Brilinta Lowers CV Risk In Patients With Prior MI



Source: Company data

Preliminary analysis did not show any unexpected safety issues. However, as noted in the editorial that accompanied NEJM publication, the 15-16% reduction in the risk of experiencing the primary end point came with a 2.3-2.7 fold higher risk of clinically significant bleeding complications. This evidence may suggest that the use of Brilinta post MI will be limited to patients with low bleeding risk.

At ESC 2017, data from a sub-group analysis was presented which showed that Brilinta 60mg BID reduced the risk of CV death by 29% (vs. placebo) in high-risk (of an atherothrombotic event) patients taking low-dose aspirin. The sub-analysis also demonstrated a risk reduction of 20% in all causes of death, and 20% in the composite of CV death, MI or stroke.

In February 2018, a sub-analysis of PEGASUS-TIMI 54 was published in the Journal of the ACC. In the design of the trial, patients with a history of MI 1-3 years before inclusion in the PEGASUS-TIMI 54 trial were stratified in a pre-specified analysis based on the presence of multivessel coronary disease (MVD). With a total of 12,558 MVD patients in PEGASUS (59.4%), a comparison of placebo-arm cohorts indicated those with MVD were at higher risk for MACE (9.37% vs. 8.57%; HR=1.24, p=0.026) and for coronary events (7.67% vs. 5.34%; HR=1.49, p=0.0005). Treatment with Brilinta demonstrated a statistically significant reduction in the risk of MACE (7.94% vs. 9.37%; HR=0.82, p=0.004) and coronary events (6.02% vs. 7.67%; HR=0.76, p<0.0001), including a 36% reduction in coronary death (HR=0.64, p=0.002).

Brilinta Fails In Stroke (Narrowly) And PAD; New Stroke Trial Initiated

In SOCRATES (n=13,199), Brilinta did not lower the risk of experiencing a CV event vs. aspirin in patients who had a prior acute ischemic stroke or a transient ischemic attack (TIA). The primary efficacy endpoint (CV death, MI, stroke) occurred in 6.7% (442/6589) of patients on Brilinta vs. 7.5% (497/6610) of patients on aspirin (HR=0.87, p=0.07). Major bleeding occurred in 0.5% of patients treated with ticagrelor and in 0.6% of patients treated with aspirin, intracranial hemorrhage in 0.2% and 0.3%, respectively, and fatal bleeding in 0.1% and 0.1%.

In EUCLID (n=13,885), Brilinta did not lower the risk of experiencing a CV event vs. generic Plavix in patients with symptomatic peripheral artery disease (PAD). The primary efficacy endpoint (CV death, MI, stroke) occurred in 10.8% (751/6930) of patients on Brilinta vs. 10.6% (740/6930) of patients on Plavix (HR=1.02, p=0.65). In each group, acute limb ischemia occurred in 1.7% of patients (HR=1.03, p=0.85). NEJM argues that Brilinta's superiority to Plavix in acute coronary syndrome (PLATO) but not in peripheral artery disease (EUCLID) might be driven by Plavix higher efficacy in PAD.

THALES (n=13,000), evaluated Brilinta and aspirin vs. placebo and aspirin in patients who had a prior acute ischemic stroke or a transient ischemic attack. Primary endpoint is time to stroke or death. Primary completion is December 2019, with data presentation expected in 2020.

Major Bleeding Risks Outweigh Benefit In Brilinta's THEMIS Trial, Expectations Trimmed To Prior-PCI Population

THEMIS (n=19,220, fully recruited as of Q2:2016) tests the hypothesis that Brilinta can lower CV risk in high risk T2DM patients vs. placebo. Positive top-line data was announced in February 2019, stating Brilinta+aspirin can significantly reduce composite of MACE compared to aspirin alone. Full data was presented at ESC in September 2019. In a median follow-up of 39.9 months, Brilinta+aspirin significantly reduced the composite primary endpoint of CV death, MI, or stroke by 10% vs. aspirin alone (7.7% vs 8.5%; HR=0.90, p=0.038). Assessment of secondary endpoints found significant reductions for MI (2.8% vs. 3.4%; HR=0.84, p=0.029) and stroke (1.6% vs. 2.0%; HR=0.80, p=0.038), but not for CV death (3.8% vs. 3.7%; HR=1.02, p=0.79). However, the efficacy benefit of Brilinta+aspirin came with a significantly higher risk for TIMI major bleeding (2.2% vs. 1.0%; HR=2.32, p<0.001), leading to a significantly higher discontinuation of study medication (4.9% vs. 1.3%, p < 0.001). In an overall composite analysis, the efficacy benefits of Brilinta+aspirin did not outweigh the bleeding risks, likely quelling adoption in the broader population.

In the THEMIS-PCI pre-specified subgroup analysis (n=11,154; patients with prior PCI), Brilinta+aspirin demonstrated a 15% risk reduction for the composite primary endpoint of CV death, MI, or stroke (HR=0.85, p = 0.013). Major bleeding risk continued to be elevated in patients with prior PCI receiving Brilinta+aspirin (2.0% vs. 1.1%, p<0.0001).

However, overall composite analysis suggested a favorable benefit/risk profile for Brilinta+aspirin within the PCI population (p=0.005), and vs. patients without prior PCI (15% relative risk reduction vs 6% relative risk increase; p=0.012). While missing an opportunity in the broader population, the combination of Brilinta+aspirin could carve out a role in treating patients with stable ischemic heart disease, T2DM, and prior PCI (an opportunity sized at 58% of the total THEMIS population, inclusive of CAD and T2DM). AZN filed Brilinta for the high-risk T2DM indication in H2:2019.

Label Warns Against Concomitant Use Of High-Dose Aspirin

The FDA confirmed that Brilinta was more effective than Plavix in preventing heart attacks and death, but that this advantage was only seen with daily aspirin doses of 75 to 100 milligrams. The Brilinta label contains a boxed warning stating that concomitant use of aspirin at doses above 100mg per days decreases the efficacy of Brilinta. An additional boxed warning stating that, "like other blood-thinning agents, Brilinta increases the rate of bleeding and can cause significant, sometimes fatal, bleeding." The most common adverse reactions reported by people taking Brilinta in clinical trials were bleeding and difficulty breathing (dyspnea) and this is also included in the labeling. Brilinta was approved with a REMS to ensure that the drug's benefits outweigh its risks. As part of the REMS, Astra must conduct educational outreach to physicians to alert them about the risk of using higher doses of aspirin. Additionally, Brilinta will be dispensed with a medication guide that informs patients of the most important information about the medication.

Epanova Approved For Severe Hypertriglyceridemia But Launch Awaits Outcomes Data

Epanova is an ultra-pure mixture of the free fatty acid forms of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), derived from fish oils. It is given as a once daily dose (2 or 4 capsules) to treat patients with severe hypertriglyceridemia (triglycerides > or = to 500mg/dL). Epanova was approved in the US in May 2014 based on data from the Phase III EVOLVE and ESPRIT trials (both conducted under an SPA), which demonstrated the effectiveness of Epanova in lowering very high triglycerides and in lowering non-HDL cholesterol in combo with a statin. Astra has initiated a CV outcomes study (STRENGTH), which will evaluate patients (n=13,086) with a TG level of 200-500 mg/dl, on statin therapy, and who are at increased risk of CV disease, treated with either Epanova + statin or corn oil + statin. Primary completion is August 2020. The primary endpoint is time to MACE. Astra plans to develop a fixed dose combination of Epanova plus a statin. Launch will occur post positive data from STRENGTH. We estimate Epanova sales of $50MM in 2021, and $250MM in 2025.

Roxadustat Achieves Top-Line In CKD Anemia; Filed In U.S.

Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) that boosts endogenous erythropoietin levels, improves iron regulation, and reduces hepcidin, a key regulator of the availability of iron for red blood cell production. In prior studies, roxadustat corrected hemoglobin (Hb) levels to within the physiological range in both CKD and non-CKD populations and in patients with high levels of inflammation without the need for exogenous iron administration. Phase III studies in China in dialysis and non-dialysis CKD patients and in Japan in dialysis patients with CKD were positive. The studies showed roxadustat's ability to correct and maintain Hb both against placebo and against ESAs with an acceptable safety profile. In China, Roxadustat was approved for dialysis-dependent CKD anemia patients in December 2018 and approved for non-dialysis CKD anemia patients in August 2019. Japan approval (as Evrenzo) for anemia associated with CKD in dialysis patients was received in September 2019. FDA filing was completed in December 2019.

Astra has rights to the U.S. and China markets (will co-commercialize with FibroGen in China). Astellas/FibroGen has rights to EU and Japan. Astra believes the novel MOA and intermittent dosing may limit the cardiovascular side effects seen with EPO. The Phase III program has been designed to demonstrate both efficacy and CV safety in dialysis patients and non-diabetic CKD patients. In September 2018, Astellas reported positive top-line results for its Phase III ALPS study (in CKD patients not on dialysis) which will support the EU filing.

In December 2018, Astra announced roxadustat top-line data in CKD-anemia for the Phase III ROCKIES (dialysis) and OLYMPUS (non-dialysis) trials, with both meeting the primary endpoint for mean change in Hb (averaged over weeks 28-52 vs. baseline). Roxadustat has potential in both the dialysis setting (where absence of CV risk is anticipated to differentiate from EPO) and pre-dialysis setting (a tougher hurdle as comparison is versus placebo, with safety a key factor). We estimate roxadustat sales of $15MM in 2019, $240MM in 2020, and $1,550MM in 2025.

Pooled Safety Data A Bit Murky, But Supportive of Filing

In May 2019, FGEN/AZN reported topline results from the pooled CV safety analyses of Roxadustat's Phase III programs in CKD. MACE was defined as a composite of all-cause mortality, stroke, and MI. MACE+ was defined as MACE plus heart failure requiring hospitalization and unstable angina requiring hospitalization. A full review of topline announcement is below; in summary, Roxadustat MACE/MACE+ risk was deemed 1) not meaningfully different from placebo in non-dialysis-dependent (NDD) patients, 2) superior to epoetin alfa in incident dialysis-dependent (ID) patients, and 3) not meaningfully different from epoetin alfa in dialysis-dependent (DD) patients already stably maintained on ESA. Although encouraging, uncertainty was created by an absence of data and undetermined statistical criteria for non-inferiority (especially in NDD patients), still under discussion with the FDA.

In a KOL call following the announcement, we learned anemia in CKD is not viewed as a major unmet need, and that safety will be more critical than efficacy for new agents. A nominal AE increase even among individual MACE components would cause our KOL to be "very discouraged". NDD CKD represents the best roxadustat value proposition and largest market but comes with the highest bar for safety. The trend toward MACE superiority in ID but not DD CKD provides little reassurance given narrow biological and temporal separation between the groups. Statistically significant results in MACE+ may be more relevant than MACE but full data are required to dispel suspicion surrounding discrepancy in results between the two composite measures.

Full Pooled Safety Data Likely To Support Approval, But Questions Remain

AZN/FGEN released pooled CV safety for roxadustat in pre-dialysis and dialysis-dependent CKD anemia showing good efficacy and comparable or reduced MACE/MACE+ risk relative to placebo and epoetin alfa, respectively. The data position roxadustat for approval but questions remain re: effects on individual MACE measures, influence of dropout rates, and prespecification of statistical endpoints.

Non-Dialysis Dependent *(vs. placebo in OLYMPUS, ALPS, ANDES; n=4,270)*

All three studies met their primary efficacy endpoints, demonstrating significant hemoglobin (Hb) increases in non-dialysis dependent (NDD) CKD patients regardless of iron repletion. NDD is the largest CKD anemia market but CV safety relative to placebo is a hurdle to approval and will determine whether roxadustat carries a black box warning. Safety endpoints were pooled across studies as each individual study was not powered for CV outcomes. Hazard ratio (HR) in time to first MACE event (composite endpoint of

stroke, myocardial infarction (MI), and all-cause mortality) is the registrational endpoint prespecified with the FDA. MACE+ (MACE plus hospitalization) is the preferred endpoint for EU filing. HR (95% CI) for composite and individual endpoints are below.

- MACE: 1.08 (0.94 - 1.24)
- MACE+ : 1.04 (0.91 - 1.18)
- All-Cause Mortality: 1.06 (0.91 - 1.23)
- Stroke: 1.22 (0.80 - 1.86)
- Myocardial Infarction: 1.28 (0.90 - 1.84)

Approval in NDD patients is made more likely by these data, but 3 key regulatory and commercial risks remain including 1) potential AdComm consideration of individual endpoints, 2) as yet unconfirmed non-inferiority thresholds, and 3) imbalance in discontinuation rates that could have favored roxadustat. Composite MACE, not individual MACE endpoints, was prespecified with the FDA as the registrational endpoint. However, the threshold for statistical non-inferiority was not prespecified with the FDA. The conventional definition of non-inferiority is HR upper bound <1.30. The pooled composite MACE and MACE+ data met that definition. The individual stroke and MI endpoints did not, and although the pooled analysis was not powered to measure the individual endpoints, they may still feature as part of a likely AdComm discussion. If approved, the higher stroke and MI HRs could be hurdles to uptake, especially if accompanied by a black box warning. One of our CKD consultants stated after the top-line release in May that a nominal AE increase even among individual MACE components would cause them to be "very discouraged". Another potential issue is that n=499 (34.4%) and n=801 (58.6%) patients discontinued roxadustat and placebo treatment, respectively, largely due to progression to dialysis. CV safety analysis was conducted in the ITT population, however, so a potentially higher number of placebo patients went on to receive epoetin alfa and may have skewed the MACE HRs in favor of roxadustat as epoetin alfa is known to be associated with MACE risk. On-treatment MACE HRs may be provided to the FDA, but it is unclear if they will look better or worse.

Dialysis Dependent (vs. epoetin alfa in ROCKIES, HIMALAYAS, SIERRAS; n=3,880)

All three studies in dialysis dependent (DD) CKD met their primary efficacy endpoints with roxadustat increasing Hb relative to baseline from week 28-52. Superiority to epoetin alfa was achieved in incident dialysis (ID) patients and statistical non-inferiority was observed in prevalent dialysis patients. Here again, CV safety is a critical factor. MACE/MACE+ endpoints were pooled across trials. HR (95% CI) for composite endpoints and mortality are below. Stroke and MI were quantified by incident rate but not assessed individually in ID patients due to sample size limitations. Endpoints with p-values noted reached statistical significance.

All DD Patients

- MACE: 0.96 (0.82 - 1.13)
- MACE+ : 0.86 (0.74 - 0.98), p=0.028
- All-Cause Mortality: 0.96 (0.79 - 1.17)
- Stroke: 2.3% roxadustat vs. 2.6% epoetin alfa
- Myocardial Infarction: 5.3% roxadustat vs. 5.6% epoetin alfa

ID Patients (n=1,526)

- MACE: 0.70 (0.51 - 0.96), p=0.029
- MACE+ : 0.66 (0.50 - 0.89), p=0.005
- All-Cause Mortality: 0.76 (0.52 - 1.11)

Approval in DD and ID patients based on non-inferior or superior efficacy and CV safety appears likely. The bar for safety is lower in this population as epoetin alfa is itself associated with MACE risk. Indeed, roxadustat was a significant improvement over epoetin alfa in some measures. For MACE and all-cause mortality in DD patients, it appears very likely that mean HRs below 1.00 combined with upper limits below the conventional 1.30 for both measures will satisfy regulators. There is the risk, however, that these less than clear-cut data, combined with potential issues in the NDD population described above, increase the likelihood of a black box warning. Discontinuation rates were again imbalanced, this time with more patients stopping roxadustat treatment (34%) vs. epoetin alfa treatment (24%). The reason according to investigators was that the trials were open label and experimental drugs are often treated more cautiously.

Roxadustat Safety Summary

	Trials	MACE (for U.S. filing)	MACE+ (for EU filing)
DD-CKD (3880 pts)	ROCKIES, HIMALAYAS, SIERRAS	HR 0.96 (0.82 - 1.13) Likely non-inferior to EPO	HR 0.86 (0.74 - 0.98), p=0.028 Superior to EPO
ID-CKD (1526 pts)	HIMALAYAS	HR 0.70 (0.51 - 0.96), p=0.029 Superior to EPO	HR 0.66 (0.50 - 0.89), p=0.005 Superior to EPO
NDD-CKD (4270 pts)	OLYMPUS, ALPS, ANDES	HR 1.08 (0.94 - 1.24) Likely non-inferior to EPO	HR 1.04 (0.91 - 1.18) Likely non-inferior to EPO

Source: Cowen and Company

Lokelma (ZS-9) Rolling Out

In December 2015, Astra acquired ZS Pharma for $2.7B cash. The lead compound is Lokelma (ZS-9), an oral treatment for hyperkalemia (elevated potassium levels in the blood often associated with CKD and CHF). ZS-9 is a proprietary zirconium silicate compound (patent protection to 2032), that is non-systemically absorbed, is odorless and tasteless, has a quick onset of action (2 hours), and is given once daily as maintenance (3x/day acutely). No significant drug-drug interactions have been seen, which is viewed as the key differentiating factor. Peripheral edema (possibly due to sodium retention) may be the most concerning side effect.

Treatment for hyperkalemia has been very limited, with the only approved drug treatments being (1) sodium polystyrene sulfonates (e.g., Kayexalate), which have many compliance and safety limitations, and (2) Relypsa's patiromer/Veltassa, a non-absorbed polymer that binds potassium in the colon; US approved in October 2015 but carries a box warning that other medications must be dosed 6 hours from patiromer dose.

Lokelma was approved in the EU in March 2018 and in May 2018 in the U.S. To date, Lokelma has been launched in a few Nordic countries, and is rolling out in the U.S. and EU. China approval was received in January 2020 (based on the HARMONIZE trial). Astra estimates peak sales for Lokelma to be $1B+. We estimate Lokelma sales of $20MM in 2019, $30MM in 2020, and $250MM in 2025.

In October 2018, AZN presented results from the Phase III HARMONIZE trial at ASN Kidney Week 2018. HARMONIZE (n=267) investigated the safety and efficacy of Lokelma vs. placebo in patients with hyperkalaemia (mean potassium levels greater than 5.0 mEq/L) in Japan, Korea, Taiwan and Russia. The study achieved its primary endpoint, in which a significantly higher percentage of patients achieved and maintained

normokalaemia on Lokelma (irrespective of dose; 5mg or 10mg) vs. placebo, with regards to mean potassium levels during days 8-29 of the maintenance phase. The results add to the growing body of evidence to support Lokelma and will provide the basis for filing abroad (filed in CN/JP with approvals expected in 2020).

In June 2019, AZN reported positive results from the Phase IIIb DIALIZE trial evaluating Lokelma efficacy and safety for treating hyperkaliemia in patients with ESRD on hemodialysis. On the primary efficacy endpoint, 41.2% of patients on Lokelma maintained pre-dialysis normal potassium levels (4-5 mmol/L), which was a statistically significant improvement vs. 1.0% on placebo. An estimated 2MM people worldwide have ESRD, placing them at higher risk for hyperkaliemia. The DIALIZE trial showed Lokelma could normalize potassium levels in between dialysis sessions for ESRD patients with hyperkaliemia.

Astra believes Lokelma is a synergistic fit with roxadustat. ZS Pharma provides a commercial sales presence targeted to nephrologists and the CKD market. In addition, Lokelma should complement Astra's CV franchise (Brilinta, Crestor) as hyperkalemia can be a side effect of CHF patients treated with RAASis (Renin-Angiotensin-Aldosterone System inhibitors) such as ACE's, ARBs, and aldosterone antagonists.

Crestor Pressured By Generic Statins

In the U.S., Actavis launched the first generic of Crestor on May 2, 2016 (post a patent settlement), and multiple other generics were launched in July 2016. Patents in the EU expired in June 2017. As a result, Crestor sales are under great pressure. We estimate Crestor sales of $1.32B (-8%) in 2019, $1.17B in 2020, and $645MM in 2025.

In December 2013, AZN settled arbitration with Shinogi over Crestor royalties and extended the period of royalty payments to Shionogi from 2016 to 2023. Under the revised terms, the payment structure was modified to reduce the royalty rate in 2014-15 by low-single digits. There will be a fixed minimum annual royalty payment from 2014 to 2020 ("low hundreds of millions of dollars") and a maximum total payment for the 2016-2020 timeframe.

Toprol XL Clipped By Generics

Toprol XL, a once-daily version of metoprolol, enjoyed great success, driven by broad use as a once-daily antihypertensive, use in CHF, and its attractive pricing. However, generics have clipped the franchise. We forecast Toprol XL sales of $730MM (+3%) in 2019, $760MM in 2020, and $925MM in 2025.

Diabetes

Diabetes Business Outlook Uncertain

In Janaury 2014, Astra acquired Bristol's portion of their diabetes collaboration and paid Bristol $3.4B in cash ($2.7B plus $0.6B for Forxiga US approval and $0.1B for Japan approval). Astra states that they have paid $4.5B in total to Bristol regarding diabetes.

The acquisition provides Astra with a strong foothold in a large and growing market and positions the company as a leading player. There are over 350MM patients WW with diabetes and this is expected to grow to 550MM by 2030. As many as 50% of all cases of diabetes remain undiagnosed, with 2/3^{rds} of these patients living in emerging

markets. We estimate the 2018 diabetes market at roughly $44B, growing to roughly $50B by 2024.

Astra/Bristol Diabetes Collaboration Background

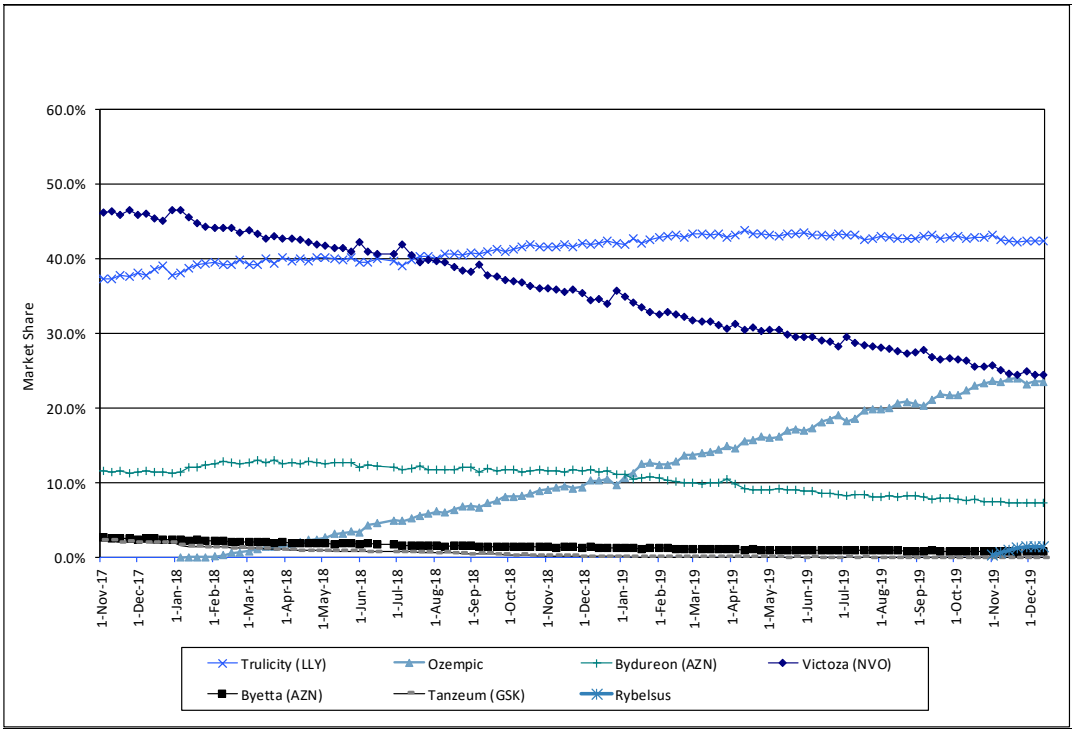
In January 2007, AstraZeneca and Bristol-Myers Squibb announced a collaboration to develop and commercialize saxagliptin (DPP IV inhibitor) and dapagliflozin (SGLT-2 inhibitor) for the treatment of Type 2 diabetes. Both compounds were discovered by Bristol-Myers Squibb. The agreements included an upfront payment of $100MM by AstraZeneca to Bristol-Myers Squibb. From 2007 through 2009, the majority of development costs were funded by AstraZeneca. Additional development costs were shared equally. Bristol-Myers Squibb was also eligible to receive additional payments of up to $650MM based on development and regulatory milestones for the two compounds. In addition, potential sales milestones up to $300MM per product were possible. The companies jointly developed the clinical and marketing strategy of the compounds, and shared commercialization expenses and profits/losses equally on a global basis, excluding Japan. Bristol-Myers Squibb had manufactured both products and booked sales. The Astra/Bristol alliance provided a wide variety of non-insulin diabetes products, including one product in each of the three fastest growing categories (DPP-IV, SGLT-2, GLP-1).

In October 2012, Bristol acquired Amylin (AMLN) Pharmaceuticals for ~$7B. Following completion of the acquisition, Bristol expanded its existing diabetes collaboration with AstraZeneca to incorporate the Amylin portfolio of products, including Byetta and Bydureon. Astra made a payment of $3.4B to Amylin as a wholly owned subsidiary of Bristol in August 2012. Profits and losses from the collaboration were shared equally between Bristol and Astra.

Bydureon Supplanting Byetta As AZN's Primary GLP-1

Byetta has struggled for several reasons, including PCP's preference to prescribe oral medications such as DPP-4s and SGLT-2s, competition from other GLP-1s, concerns over pancreatitis, complex issues surrounding reimbursement, and an inconvenient twice daily dosing. Bydureon is exenatide (Byetta) encapsulated in proprietary microspheres that allows slower release and a once weekly dosing. Bydureon was first-to-market once-weekly GLP-1 analog. Given the sheer size of the diabetes market and the added convenience, Bydureon has the potential to become a $1B+ drug over time. However, competition is intensifying as Trulicity (LLY) has been impressive and once weekly Ozempic (NVO) is rolling out. Bydureon and Byetta combined currently hold approximately 7.8% NRx share of the U.S. GLP-1 market.

GLP-1 Current U.S. Market Share



Source: IQVIA

Bydureon was studied in a robust clinical program that included monotherapy and combinations with metformin, sulfonylurea and thiazolidinedione. In monotherapy, Bydureon showed HbA1c reductions superior to Januvia and non-inferior to metformin. As add-on to metformin±sulfonylurea, Bydureon showed HbA1c reductions superior to Januvia and Byetta and non-inferior to pioglitazone. However, Bydureon failed to show non-inferiority to Victoza (GLP-1 market leader) in patients on metformin±sulfonylurea/ pioglitazone. This study put Bydureon at a competitive disadvantage to Trulicity (LLY), which showed non-inferiority to one daily Victoza.

Bydureon's single chamber auto-injector pen, Bydureon BCise, was approved in the U.S. in October 2017 (launched January 2018) and in the EU in August 2018. The approval/filing was based on DURATION-NEO-1 which showed non-inferiority to Byetta. Astra estimates that over half of BCise users are new to the GLP-1 class and about a third are coming from a switch from the old Bydureon pen. Supply constraints have hampered recent trends, but normal supply was reestablished in 2019.

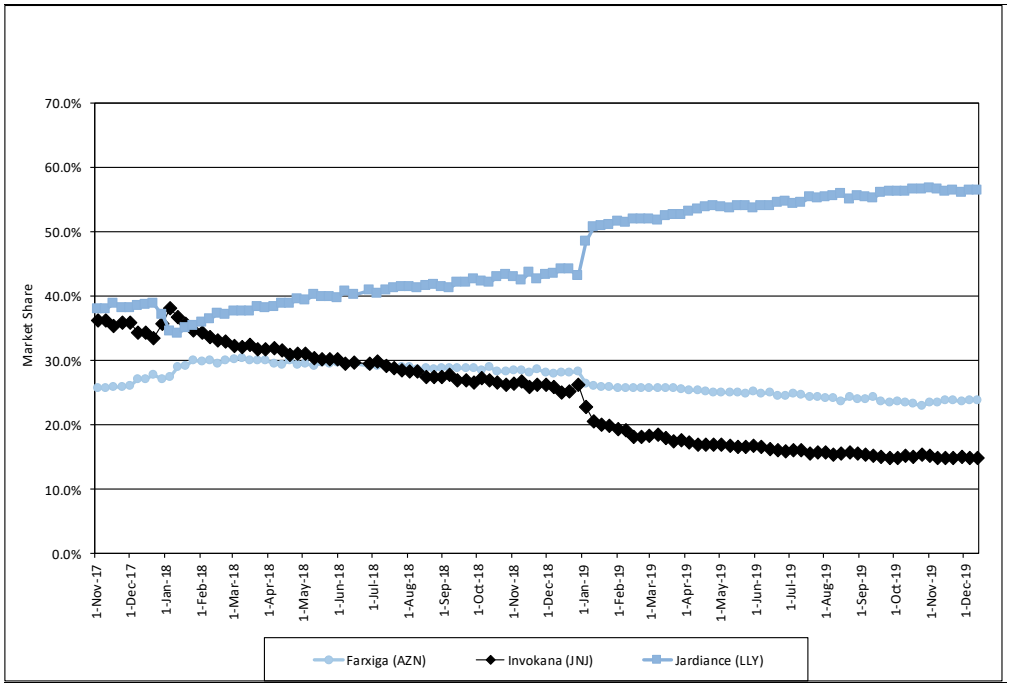
In May 2017, top-line data from Bydureon's long-term CV outcomes trial EXSCEL (n=14,500) was announced, showing that Bydureon met the primary safety endpoint and did not increase the risk of MACE (HR=0.91; CI: 0.83-1.00; p<0.001 for non-inferiority), but also did not show a statistically significant reduction in MACE (as expected). Full data, presented at EASD:17 (September), showed there were fewer CV events in the Bydureon arm (839 vs. 905 for placebo), although statistical superiority was not reached (p=0.061). In a pre-specified secondary analysis, Bydureon patients showed a 14% lower incidence of death from all causes. The EXSCEL data is now in both U.S. and EU labels.

We estimate Bydureon sales of $545MM (-7%) in 2019, $555MM in 2020, and $730MM in 2025.

Farxiga Inroads Driven By Appeal Of SGLT-2 Class, Positive CV Data

Dapagliflozin (Forxiga in EU/Farxiga in U.S.) is Astra's once-daily SGLT-2 inhibitor. In July 2011, the FDA AdCom voted 6-9 against approval, stating that a sufficient risk-benefit ratio had not been established. In January 2012, FDA issued a complete response letter requesting additional data. Concerns focused on possible imbalances in CV events, bladder cancer, breast cancer and liver toxicity in certain subgroups. Astra refiled in July 2013 and received a favorable AdCom in December 2013. CV risk profile was viewed as acceptable, bladder cancer risk considered minimal, and liver toxicity concerns alleviated. Approval was granted in November 2012 in the EU, January 2014 in the U.S., March 2014 in Japan, and March 2017 in China. A fixed dose combination with metformin (Xigduo) is available in all major markets.

U.S. SGLT-2 Inhibitors Market Shares



Source: IQVIA . Invokana includes FDC with metformin (Invokamet), Jardiance includes FDC with metformin (Synjardi) and Tradjenta (Glyxambi). Farxiga includes FDC with metformin (Xigduo)

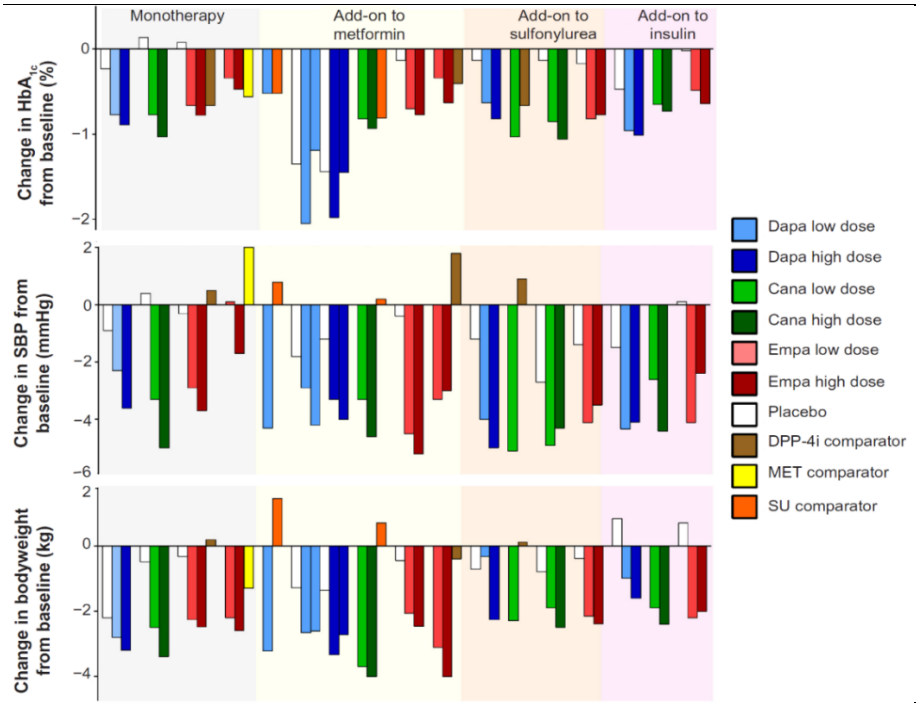
Key drivers for long-term growth include: 1) label update for positive CV outcomes data (DECLARE); approved in EU in August 2019 and U.S. in October 2019; 2) label update for HFrEF (DAPA-HF), PDUFA Q2:20, 3) outcome studies in chronic kidney disease (Dapa-CKD; n=4,000, primary completion November 2020; granted Fast Track status August 2019); and 4) use in T1DM; Forxiga was approved for T1DM in the EU and Japan in March 2019; a CRL was received in the U.S. in July 2019. We estimate Farxiga sales of $1.555B (+12%) in 2019, $1.7B in 2020, and $2.41B in 2025.

Reduction In HbA1c, Body Weight And Blood Pressure In Line With The Class

Farxiga is approved based on a robust clinical program that tested it as monotherapy, or as add-on to metformin, pioglitazone, sulfonylurea, sitagliptin and insulin. Overall,

Farxiga showed reductions in A1c, body weight and systolic blood pressure in line with the class. Reduction in body weight and systolic blood pressure are meaningful for the class given metformin and DPP-4 do not have such benefit. A comparison of the clinical data reported so far for the class is below.

Reductions In HbA1c, Body Weight And Systolic Blood Pressure Across The SGLT-2 Class



Source: Company data

AZN also notes distinctions between SGLT2's and GLP1's. GLP1's have higher glucose reduction; however, weight loss is less consistent. SGT2's deliver more consistent weight loss. The key differences are in CV outcomes, where GLP1's show MACE improvement in about 10% of patients, whereas SGLT2's show MACE improvement in 40-50%.

Qtern (Farxiga/Onglyza/Metformin) Combos Approved In EU And U.S.

Phase III (n=534) data for Farxiga+Onglyza (SGLT-2+DPP-4) showed superior HbA1c control vs. either drug alone in patients poorly controlled on metformin. HbA1c reduction at 24 weeks was 1.47% for the combo, 0.88% for Onglyza and 1.2% for Farxiga. Importantly, 41% of the patients on the combo were on goal (A1C < 7%) at study completion. AstraZeneca believes that the oral combination can delay insulin initiation. . The combination was approved in Europe in July 2016 and in the U.S. in February 2017. Triplet combination of Forxiga/Onglyza/metformin (Qternmet XR) was approved in the U.S. in May 2019 and in the EU in November 2019 (as Qtrilmet).

T1DM: Approved In EU/JP As Insulin Adjunct, CRL Issued In The U.S.

The Forxiga DEPICT-1 24-week data (presented at EASD:17) showed improved glycemic control, weight loss, and no increased incidence of ketoacidosis in T1DM. DEPICT-2 24-week data for 5mg and 10mg Forxiga plus insulin (presented at ADA'18) was also positive: Forxiga 5mg + insulin showed -0.34% reduction in HbA1c (-0.37% from baseline, p=0.0001), and 10mg + insulin showed -0.39% (-0.42% from baseline,

p<0.0001); both doses met demonstrated significant improvements for key secondary endpoints including decreased daily insulin dosage, decreased body weight, decreased 24-hour CGM glucose reading, decreased 24-hour glucose excursion, and increased 24-hour intestinal glucose. Forxiga was approved in the EU and Japan in March 2019 for use as adjunct to insulin T1DM (in patients with BMI >/= 27 kg/m^2).

In July 2019, the FDA issued a CRL regarding the sNDA for Farxiga as an adjunct to insulin in T1DM adults, when insulin alone does not provide adequate glycemic control. AZN commented that it is working closely with the FDA to discuss next steps.

DECLARE Provides A Boost To Farxiga And SGLT-2 Class

Full results of DECLARE-TIMI 58, the CV outcomes trial for Farxiga vs. placebo, were presented at AHA 2018. Results were simultaneously published in the New England Journal of Medicine (NEJM), and a meta-analysis was published in Lancet. DECLARE included 17,160 patients across 33 countries. DECLARE is distinguished from other SGLT2 CV trials in that a large percentage (59%) of patients were primary prevention. Forxiga significantly reduced the risk of hospitalization for heart failure or CV death vs. placebo by 17% (4.9% vs. 5.8%; HR 0.83, p=0.005), one of the two primary efficacy endpoints. The reduction in the endpoint was consistent across the patient population, included those with CV risk factors and those with CV disease.

The second primary endpoint for MACE showed a trend favoring Farxiga but it did not reach statistical significance (8.8% for Farxiga vs. 9.4% for placebo; HR 0.93, p=0.17). The trend in the endpoint was not consistent across the patient population; those with CV disease saw a 10% benefit while those with CV risk factors had a neutral impact. Given that only one of two primary endpoints was achieved, analysis of secondary endpoints was not possible. However, a renal composite endpoint (4.3% for Farxiga vs. 5.6% for placebo; HR 0.76, p<0.001) and all-cause mortality (6.2% for Farxiga vs. 6.6% for placebo; HR 0.93, p=0.20) showed positive trends. The safety profile showed no imbalance for Farxiga vs. placebo in amputations (1.4% vs. 1.3%), fractures (5.3% vs. 5.1%), bladder cancer (0.3% vs. 0.5%) or gangrene (1 case vs. 5 cases). Diabetic ketoacidosis (0.3% vs. 0.1%) and genital infections (0.9% vs. 0.1%) occurred more frequently on Farxiga but were rare.

At the ACC meeting in March 2019, AZN announced positive results from a pre-specified sub-analysis of DECLARE-TIMI 58, showing Farxiga reduced the relative risk of MACE by 16% compared to placebo in T2DM patients who had a prior MI. In addition, Farxiga reduced the relative risk of hospitalization for HF in patients with T2DM regardless of their EF status, a measurement of the percentage of blood leaving the heart with each contraction. These pre-specified sub-analyses add to the positive primary results of the trial presented at the AHA in November 2018.

DECLARE was a success for Farxiga and in line with CV outcomes results for other SGLT2's. The primary prevention cohort is an added benefit that will be considered a class effect. The meta-analysis published in Lancet is strong evidence that SGLT's prevent heart failure/CV death in patients without preexisting ASCVD and in those with ASCVD also reduce MACE. This data will continue to elevate this class to first line, perhaps even before metformin for T2DM. The MACE benefits of SGLT2's and GLP1's are similar, but SGLT2's appear to have the edge on heart failure outcomes.

Farxiga Uptake In T2DM Should Benefit From Updated Guidelines

In 2018, the ADA updated its Standards of Medical Care in Diabetes with new drug therapy recommendations for antihyperglycemic therapy for adults with T2DM, to reflect recent CV outcomes trials. The 2018 guidelines endorse that people with

atherosclerotic cardiovascular disease (ASCVD) should begin with lifestyle management and metformin, then and subsequently incorporate an agent proven to reduce MACE and/or CV mortality after considering drug-specific and patient factors. As such, the ADA recommends that such patients be considered candidates for either a GLP-1 agonist or SGLT-2 inhibitor to lower the risk of death. In November 2018, the ACC also endorsed SGLT2 inhibitors given their proven benefit in reducing risk of cv death in adults with T2DM and established CV disease. The 2019 ADA Guidelines continue to reflect the recommendation of prescribing an SGLT2 inhibitor or GLP-1 agonist with proven CV benefit to patients with clinical CV disease. Based on the review of recent data, the 2019 ADA Guidelines also recommend an SGLT2 inhibitor with proven benefit for patients with CKD or clinical HF and ASCVD.

Farxiga Reduces CV Death Or Worsening HF For HFrEF Patients In Phase III DAPA-HF

In August 2019, AZN announced top-line results from the Phase III DAPA-HF trial – the first HF outcomes trial with an SGLT2 inhibitor in patients with and without T2DM. Full results were presented at ESC in September 2019. The randomized, controlled study evaluated Farxiga (10mg once-daily in addition to SOC) vs. placebo in patients with chronic HF and reduced ejection fraction (HFrEF), both with and without T2DM (n=4,744). Farxiga met the primary composite endpoint, demonstrating a significant reduction of CV death or worsening of HF (defined as hospitalization or urgent HF visit; HR=0.74, p<0.00001). A component analysis of the primary endpoint showed Farxiga significantly reduced the probability of both worsening HF (HR=0.70, p=00003) and CV death (HR=0.82, p=0.029). Farxiga also met key secondary endpoints for total HF hospitalizations and CV death (including first and repeat hospitalizations; HR=0.75, p=0.0002), as well as all-cause mortality (HR=0.83, p=0.022). Safety was reportedly consistent with previous dapagliflozin trials. Farxiga was well-tolerated in diabetics and non-diabetics, and also demonstrated a significant reduction of serious AEs (p<0.01).

A subgroup analysis showing impressive efficacy in patients with T2DM (HR=0.75) and without T2DM (HR=0.73) demonstrated the SGLT2 inhibitor is efficacious for treating HF in addition to treating diabetes, providing additional clout for label expansion. In a post-presentation analyst call, AZN highlighted that Farxiga also demonstrated significant reductions in the composite primary endpoint for patients with either NYHA class II HF (HR=0.63) or LVEF >median (HR=0.81). Another subgroup analysis showed Farxiga had consistent efficacy in HFrEF patients regardless if they were taking an angiotensin receptor neprilysin inhibitor (HR=0.75) or not (HR=0.74), opening the possibility for combination treatment with Entresto (NVS). Farxiga is also being studied in HFrEF in DETERMINE-reduced (n=312, primary completion February 2020), as well as in HFpEF in both DETERMINE-preserved (n=500; primary completion July 2020) and DELIVER (n=4,700; CV outcomes trial; primary completion June 2021).

Onglyza Sales In Decline; Sales Support Limited

Onglyza (saxagliptin)'s efficacy appears in line with the class and offers one downward dose adjustment in patients with CKD instead of two for Januvia. However, Onglyza also has more drug-drug interactions vs. Januvia as it inhibits the CYP3A4/5 pathway. Fixed dose combination with metformin (Komboglyze) are available in all major markets. Warning and precautions of the label include risk of acute pancreatitis and heart failure. These risks reflect post-marketing reports and Onglyza's CV study showing a statistically significant 27% increase in risk of hospitalization for HF. While the risk of pancreatitis is a common warning across the class, the increased risk of HF may limit Onglyza growth as Januvia does not have such signal and other drugs (GLP-1/SGLT-2) have shown a benefit. In 2017, Astra removed sales support in the U.S. to direct

resources to other products. We estimate Onglyza sales of $530MM (-2%) in 2019, $475MM in 2020, and $200MM in 2025.

Respiratory/Inflammatory/Autoimmune

Symbicort Generics A Risk In U.S.; Generic Marketed In EU

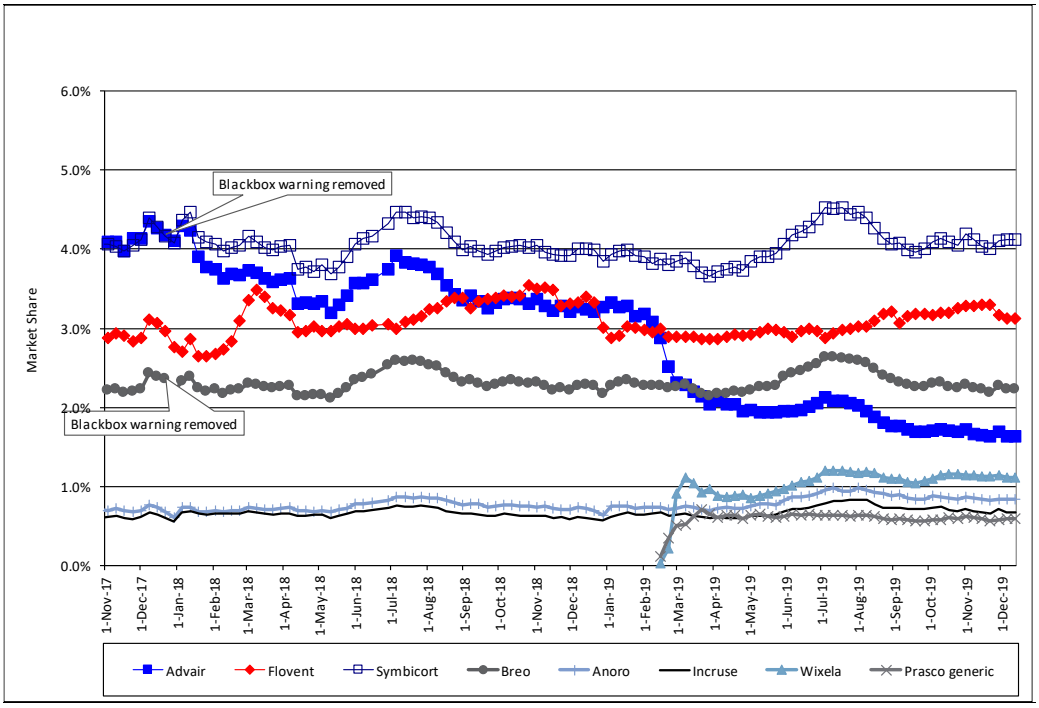
Symbicort is a twice-daily, inhaled combination of budesonide (ICS) and formoterol (LABA) indicated for the treatment of asthma and COPD. AstraZeneca launched Symbicort pMDI (80/4.5mcg and 160/4.5mcg) in the U.S. in July 2007 for the maintenance treatment of asthma in patients age 12 and older. In February 2009, the FDA approved Symbicort 16/4.5 mcg for maintenance therapy in COPD including emphysema and chronic bronchitis. In January 2017, use in pediatric asthma was expanded to include ages 6-12 y.o. (at 80/4.5 dose). In September 2017, the FDA approved an update to the Symbicort label for use in prevention of COPD exacerbations.

Budesonide is an important alternative inhaled steroid, given that it shares Flovent's (fluticasone) efficacy but with less systemic absorption. Additionally, patients might benefit from the faster onset of action of formoterol, the long-acting beta agonist in Symbicort (as opposed to salmeterol, the long-acting beta agonist in GlaxoSmithKline's Advair). This has potential utility in an acute asthmatic attack. However, other than these two attributes, there appears to be little to distinguish Advair from Symbicort.

In late 2014, Astra initiated two Phase III studies (SYGMA1, 2; n=8,065 for both) to evaluate Symbicort in mild asthma used on an "as needed" basis. In May 2018, Astra announced that both trials met their primary efficacy endpoints, indicating that "as needed" Symbicort provides at least similar asthma control and exacerbation reduction compared to standard maintenance treatment with less ICS exposure; symptom control was shown to be not as effective as maintenance treatment. Nonetheless, "as needed" Symbicort use appears to offer a new beneficial treatment regimen. Symbicort was expected to be filed for mild asthma in China by YE 2019 and to be filed in the EU in 2020.

There are a number of Symbicort generics and analogues approved in the EU, although sales have held up relatively well (company estimates ~28% share vs. 8% for analogues). Symbicort is also now facing generic competition in Japan. In the U.S., Symbicort has eight patents that expire during 2017 to 2029. Mylan/3M had indicated plans to file their generic Symbicort in 2018 and "launch at earliest opportunity", but no further updates have been provided. We forecast Symbicort sales of $2.395B (-6%) in 2019, $2.185B in 2020, and $1.16B in 2025. Admittedly, our estimates are at risk pending additional visibility on generic competition.

Asthma/COPD Market



Source: IQVIA

Pulmicort Supported By Emerging Markets

Pulmicort (budesonide) is an inhaled corticosteroid indicated for maintenance treatment of asthma in children and adults. In some countries, Pulmicort is also indicated for maintenance treatment of COPD. Pulmicort is available in three administration forms: Pulmicort Turbuhaler, a dry powder inhaler; Pulmicort Respules, a nebulizing suspension; and Pulmicort pMDI, a pressurized metered-dose inhaler. Generics have been available in the U.S. since 2015. However, Pulmicort has been quite successful in Emerging Markets, particularly China, where AZN has invested in nebulization centers.

Pulmicort sales are forecast to be $1.45B (+13%) in 2019, $1.5B in 2020, and $1.7B in 2025.

Tudorza And Duaklir U.S. Rights Acquired By Circassia

In November 2014, Astra acquired the rights to Almirall's respiratory portfolio which included Tudorza/Eklira (twice daily LAMA aclidinium in a DPI device, approved for COPD in the U.S. and EU) and Duaklir (twice daily LAMA/LABA aclidinium/formoterol in a DPI device approved for COPD in the EU). In March 2017, Astra entered a collaboration with Circassia Pharmaceuticals for the development and commercialization of Tudorza and Duaklir in the U.S. Astra received $50MM in ordinary shares of Circassia at closing and $100MM when Duaklir was approved in the U.S. Income from Circassia is reported in Externalization Revenue.

Duaklir was approved for COPD in the U.S. in March 2019 based on the positive Phase III (AMPLIFY) data reported in September 2017. Circassia will pay Astra tiered royalties on future U.S. Duaklir sales.

For Tudorza, Circassia will lead promotion in the U.S. with an option to gain full commercial rights (for $80MM). In March 2019, the FDA approved a label update to include cardiovascular safety and exacerbation data from the Phase IV ASCENT trial. The two companies will share U.S. Tudorza profits equally; Astra will continue to book U.S. Tudorza sales (until option exercised).

We estimate Tudorza/Eklira sales of $85MM (-23%) in 2019, $105MM in 2020, and $205MM in 2025. We estimate Duaklir OUS sales of $80MM (-16%) in 2019, $85MM in 2020, and $135MM in 2025.

OUS Rights To Daliresp Acquired

In Q1:2016 Astra acquired Takeda Pharmaceutical's respiratory business for $575MM. The transaction included the OUS rights to Daliresp (roflumilast; oral PDE4 inhibitor for COPD); Astra had acquired the US rights to Daliresp in Q1:15 from Actavis. Astra gains access to other marketed and pipeline respiratory products. We estimate Daliresp sales of $210MM (+11%) in 2019, $235MM in 2020, and $335MM in 2025.

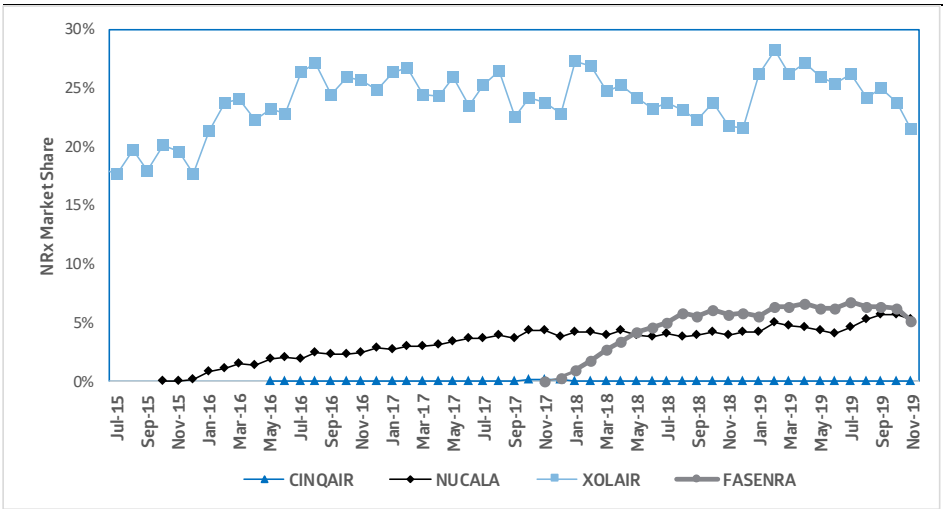
Fasenra Gaining Share For Severe Asthma, COPD Trials Fail

Fasenra (benralizumab) is an anti-IL-5Rα antibody targeting asthmatics with eosinophils (represents ~40-60% of severe asthmatics). Given that high eosinophil count is associated with asthma exacerbations, depleting eosinophils by blocking IL-5Rα is a logical strategy for the treatment of severe asthma. Benralizumab binds the alpha chain of the interleukin 5 (IL-5) receptor and produces apoptosis via antibody-dependent cellular cytotoxicity. Astra believes targeting the receptor is superior to targeting the ligand. Fasenra advantages include dosing convenience (Q8W vs. Q4W), a pre-filled syringe, and demonstrated benefits in oral corticosteroid (OCS) reduction. Astra estimates that less than 1 in 10 asthma patients eligible for a biologic receive one, suggesting sizable market upside.

Fasenra was U.S. approved in November 2017, and in the EU and Japan in January 2018, as add-on maintenance for severe asthma patients (age 12yo +) with an eosinophilic phenotype at a dose of 30mg Q4W for 3 doses, and then 30mg Q8W thereafter. Fasenra is priced (WAC) at $38K for the first year, and $28-33K per year thereafter (depending on timing of doses). This is on par with GSK's Nucala which is priced at approximately $33.5K per year (Q4W SC dosing). EU approval for severe eosinophilic asthma was received in January 2018 but with the added restriction of failure on high dose inhaled corticosteroids plus LABAs. In July 2019, an auto-injector pen device was approved in the EU; U.S. approval was granted in October 2019.

Fasenra has had a strong launch and is gaining the newest patients. Astra believes Fasenra's profile accounts for the quick uptake, with particularly positive feedback from patients regarding consistency in effect of treatment. Management is seeing the strong uptake across geographic areas including the U.S., Germany, and Japan (where it may be the strongest). One of the biggest hurdles to overcome in the space is that patients are misdiagnosed and are stuck in primary care, causing an over-reliance on oral steroids that often compromise treatment.

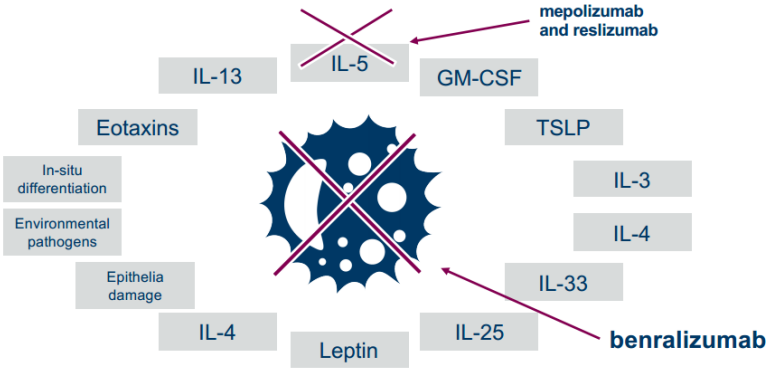
Anti-IL-5 Asthma Drugs



Source: Cowen and Company

In Q2:18, Astra announced that both Phase III trials in moderate to very severe COPD did not meet their primary endpoint of exacerbation reduction. A Phase III trial in nasal polyposis (OSTRO, n=409) was initiated in Q2:2018 (primary completion is August 2020). Fasenra is also starting Phase II/III for HES (hypereosinophilic syndrome) and is in Phase II for EGPA (eosinophilic granulomatosis with polyangiitis); the FDA granted Orphan Drug designation for both these indications. In August 2019, the FDA also granted Orphan Drug Designation for use in eosinophilic oesophagitis. We estimate Fasenra sales of $725MM (+144%) in 2019, $1,060MM in 2020, and $2,420MM in 2025.

Benralizumab MOA



Source: AstraZeneca

Phase III Data In Asthma Strong

A Phase III trial (Windward program) began in October 2013. The two pivotal studies were CALIMA (n=1,300+), and SIROCCO (n=1,134) in adults/adolescents with severe asthma inadequately controlled on high-dose steroids and LABAs and experiencing at least 2 exacerbations in the prior 12 months. Positive top-line data was announced in May 2016 as both trials met their primary endpoint of reduction in annual exacerbation rate vs. placebo. In Q3:16, positive top-line data was reported for ZONDA (n=210), an oral corticosteroid reducing trial in adults with severe asthma inadequately controlled

on high-dose steroids/LABA and other chronic oral steroid therapy; full data presented in May 2017 showed 66% of benralizumab patients were able to decrease OCS use by at least 50% vs. placebo when the median reduction in OCS dose was 75% vs. 25% for placebo; a 70% reduction in annual exacerbation rate was also reported. Data from the Phase III BORA (n=1,926) long-term safety extension trial was announced in September 2018, which showed that 74% of high-eosinophil asthma patients (300 cell/μL or greater) who received Fasenra Q8W were exacerbation-free in their second year of treatment and also maintained improved lung function. However, the Phase III SOLANA (n=235) trial in patients with severe uncontrolled asthma with eosinophilic flares did not meet its co-primary endpoint of FEV1 and RV (lung function measures).

Full data from SIROCCO and CALIMA were presented at ERS 2016 (Sep). In both studies, benralizumab reduced annual exacerbation rates and improved lung function. Quality of life measures were also favorable. The incidence of side effects was similar to placebo in both groups. The efficacy results of the Q8 week regimen were similar to the Q4 week schedule, although the Q8W dosing showed greater improvement in the sub-group of patients with ≥3 prior exacerbations in the past year. The data suggests a potentially more favorable Q8 week dosing regimen may be possible for at least some patients.

SIROCCO And CALIMA Summary Results

	SIROCCO (48 wks)			CALIMA (56 weeks)		
	Q4W	Q8W	Placebo	Q4W	Q8W	Placebo
Dose	30mg SQ	30mg SQ	--	30mg SQ	30mg SQ	--
Enrollment	403	394	407	438	428	440
Exacerbation Rate Change Vs Placebo						
Overall*	-45%	-51%	--	-36%	-28%	--
Pts w/ ≥3 prior exacerbations	-46%	-57%	--	-45%	-51%	--
FEV1 Vs Placebo						
Overall*	+106ml	+159ml	--	+125ml	+116ml	--
Pts w/ ≥3 prior exacerbations	+108ml	+235ml	--	+151ml	+265ml	--
Adverse Rxns						
Any	72.7%	71.3%	76.4%	73.5%	74.8%	77.7%
SAE	11.7%	13.2%	13.5%	10.3%	9.3%	13.6%
Discontinuation	2.2%	2.0%	0.7%	1.8%	2.3%	0.9%
Injection Site Rxns	4.0%	2.3%	2.0%	2.5%	2.1%	1.8%
Hypersensitivity	3.2%	2.8%	2.7%	3.0%	3.5%	4.1%

* All enrollees had ≥2 exacerbations in prior 12 months

Source: Company data

At ERS:17, AstraZeneca presented a subgroup analysis of the SIROCCO and CALIMA trials which showed that severe asthma patients which had 1) high baseline blood eosinophil count, 2) a history of more frequent exacerbations, 3) use of oral corticosteroids, and/or 4) nasal polyposis, were more likely to have a better treatment response to benralizumab.

Both Phase III COPD Trials Miss Endpoint

Astra initiated the Phase III VOYAGER program in Q2:14 evaluating benralizumab in patients with moderate to very severe COPD and high risk of exacerbations. The two pivotal studies are GALATHEA (n=1,656) and TERRANOVA (n=2,255). Patients included have a wide range of eosinophil levels. The primary endpoint is reduction in rate of exacerbations; the secondary endpoints include FEV1 and quality of life measures. In

May 2018, Astra announced that neither trial met the primary endpoint of a statistically significant reduction in exacerbations. Safety and tolerability were consistent with prior studies of Fasenra. Data from both studies is being analyzed (and will be presented at a future medical meeting), but there are no plans for regulatory filings.

Bevespi (LAMA/LABA) Approved For Twice Daily Use In U.S. And EU

Bevespi Aerosphere (PT003) is a twice-daily, fixed dose combination of glycopyrronium (LAMA) and formoterol fumarate (LABA) delivered in a pMDI using a novel co-suspension formulation technology. Bevespi is the lead compound from the June 2013 acquisition of Pearl Therapeutics. In April 2016, Bevespi was approved for COPD in the U.S.; EU approval received December 2018; and Japan approval in June 2019. We estimate Bevespi sales of $45MM (+36%) in 2019, $75MM in 2020, and $325MM in 2025.

Disappointing Results In Phase III Comparison To GSK's Anoro

The Phase IIIb AERISTO (n=1,119) evaluated twice daily Bevespi to once-daily LAMA/LABA Anoro (GSK; umeclidinium/vilanterol) in patients with COPD. In August 2018, Astra reported mixed top-line results for the trial's three primary endpoints: Bevespi did demonstrate non-inferiority on peak change from baseline in FEV1 but did not demonstrate superiority on FEV1 or non-inferiority on trough FEV1. Management is reviewing the data and noted that the results are inconsistent with previous data. Full data will be presented at a future medical meeting.

COPD Filings Supported By Phase III PINNACLE Trials

In March 2015, positive top-line results from the global Phase III PINNACLE study in COPD were announced. In PINNACLE-1 and PINNACLE-2, PT003 met the primary endpoint of improvement in FEV1 at 24-weeks compared to the individual components and placebo. The most common AEs were nasopharyngitis, URI, and dyspnea; the incidence was similar across all treatment groups. In October 2017, positive top-line data from PINNACLE-4 (n=1,756) was announced in which Bevespi showed a statistically significant improvement in FEV1 compared to its individual components at 24 weeks.

Breztri (PT010 Triple Therapy) Approved In Japan/China; Under Review In EU; CRL Received In U.S.

Breztri Aerosphere (PT010) is a triple therapy ICS/LAMA/LABA (budenoside/glycopyrronium/formoterol) in a pMDI device, was approved in Japan in June 2019 and China in 2019 for COPD. Breztri is under review in the U.S. and EU; however, in October 2019, PT010 received a CRL from the FDA; Astra plans to submit additional data (ETHOS; only KRONOS data included in initial submission) and continues to expect approval in H1:20.

Filings were supported by the Phase III trials (ATHENA program) for moderate to severe COPD. In January 2018, Astra reported positive data from the Phase III KRONOS trial (n=1,800) in which PT010 met 6 of the 7 lung function superiority primary endpoints. In August 2019, positive top-line results from the Phase III ETHOS trial (n=8,000) were announced; the primary endpoint is rate of exacerbations vs. dual therapy. ETHOS and TELOS include low and high doses of ICS and stratify patients by eosinophil level. AZN believes Breztri's device (Aerosphere pMDI), product formulation, and twice-daily dosing will be key differentiating factors, and that budesonide (steroid) has unique

characteristics. Breztri is also in Phase II for asthma. We estimate Breztri sales of $5MM in 2019, $50MM in 2020, and $300MM in 2025.

KRONOS Trial Demonstrates Lung Function Benefits In COPD

In January 2018, Astra reported KRONOS Phase III data. KRONOS is a 24-week trial evaluating PT010 (budenoside/glycopyrronium/formoterol 320/14.4/9.6g) vs. Symbicort, Bevespi, and PT009 (budenoside/formoterol 320/9.6g). All patients received 2 inhalations twice a day of each product. PT010 met the superiority primary endpoint of FEV1 in 6 of the 7 lung function evaluations and both non-inferiority endpoints vs. dual combination therapies. In addition, PT010 cohorts demonstrated a statistically significant 52% reduction in exacerbations compared to Bevespi and 18% and 17% reductions, respectively, to PT009 and Symbicort (not stat sig). There were no unexpected safety or tolerability signals. The incidence of pneumonia was low (1.9%) and comparable across all treatment arms (1.6% for Bevespi, 1.9% for PT009, and 1.3% for Symbicort).

KRONOS Trial Primary Endpoints

Summary of trial results:

Primary endpoint results assessed by FEV1	
PT010 vs *Symbicort*	
Over 24 weeks (post-dose*)	Met
PT010 vs *Bevespi Aerosphere*	
Over 24 weeks (trough)	Met
Over 12-24 weeks (trough)	Met
At 24 weeks (trough)	Not met; favourable trend
PT010 vs PT009	
Over 24 weeks (post-dose*)	Met
Over 12-24 weeks (trough)	Met
At 24 weeks (post-dose*)	Met
PT009 vs *Symbicort* (non-inferiority comparison)	
Over 24 weeks (trough)	Met
Over 12-24 weeks (trough)	Met

* Post-dose assessments FEV1 area under the curve 0-4 hours

Source: AstraZeneca

Tezepelumab Phase II Data In Severe Asthma Impressive

Tezepelumab/MEDI9929 is an anti-TSLP (thymic stromal lymphopoietin) mAb. TSLP is an upstream mediator of inflammation in asthma. Blocking TSLP may prevent the release of inflammatory cytokines and thus prevent asthma exacerbations and improve asthma control. Because of activity early in the inflammation cascade, tezepelumab may be suitable for both T2 and non-T2 driven asthma (T2 accounts for ~ 2/3rds of severe asthma patients, non T2 1/3rd).

A Phase I study showed tezepelumab reduced allergen-induced bronchoconstriction and airway inflammation with an acceptable safety profile. No dose-limiting toxicity was observed. In Q1:17, Astra announced that the Phase II study (PATHWAY; n=552) in severe asthma met its primary endpoint of reduction in exacerbation rate. Full data presented in September 2017 (and published in NEJM), showed that tezepelumab reduced the annual asthma exacerbation rate by 61%, 71%, and 66% for doses of 70mg Q4W, 210mg Q4W, and 280mg Q2W, all vs. placebo. These reductions were seen regardless of baseline eosinophil count or other T2 inflammatory biomarkers. Tezepelumab also demonstrated improvements in lung function at all doses and in asthma control at the two higher doses. Adverse events were similar across all

tezepelumab doses and placebo, with most common AEs (>5%) were asthma, nasopharyngitis, headaches, and bronchitis. In September 2018, tezepelumab received Breakthrough Therapy Designation for severe asthma, without an eosinophilic phentotype.

The first Phase III trial in severe asthma (NAVIGATOR, part of PATHFINDER program) has initiated and will enroll 1,060 patients (adults/adolescents). Primary endpoint is annualized exacerbation rate; primary completion is September 2020. We estimate tezepelumab sales of $50MM in 2022 and $150MM in 2025.

Our consultants view this early data as very attractive since the impact is upstream in the inflammatory pathway and can impact both T2 and especially the non-T2 pathway where effective treatment is much needed.

Anifrolumab Misses Endpoint In First Phase III Trial For SLE; Hits In Second

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Anifrolumab targets IFN alpha receptor and inhibits the activity of all type I IFNs. In August 2015, anifrolumab received Fast Track designation from the FDA for SLE. In November 2015, Astra presented positive data from the Phase II MUSE trial (n=305) and demonstrated reduced lupus activity compared to placebo. Anifrolumab was dosed at either 300mg or 1000mg IV Q4W for 48 weeks. Primary and secondary endpoints were met for all doses. Serious AEs were reported in 16.7% of anifrolumab patients vs. 18.8% for placebo. In anifrolumab patients, there was a dose-dependent increase in herpes zoster (9.5% for 1000mg, 5.1% for 300mg, 2% for placebo) and a greater number of influenza infections (most unconfirmed). There was also greater efficacy in patients with high IFN gene signatures. SLE is an extremely difficult disease in which to show benefit in clinical trials, but nonetheless, our KOLs were optimistic about anifrolumab.

In Q3:15, Astra initiated two Phase III trials (TULIP-SLE1 and TULIP-SLE2, n= 810 combined; 300mg maximum dose) in moderate-to-severe SLE. However, in August 2018, Astra announced that the primary endpoint of SLE Responder Index 4 (SRI4) in TULIP-1 was not reached. However, in August 2019, Astra announced that the primary endpoint in TULIP-2, British Isles Lupus Assessment Group based Composite Lupus Assessment (BICLA) was met and indicated that the positive BICLA was consistent with a prespecified analysis in the TULIP-1 trial. Given the large unmet need, Astra is hopeful to work with regulators on a path forward. Anifrolumab is also being evaluated for lupus nephritis (in Phase II; primary completion November 2019) and as a SQ formulation (Phase II). We estimate anifrolumab sales of $10MM in 2022 and $40MM in 2025.

TULIP Data

Anifrolumab met KOL expectations for efficacy in TULIP-2. TULIP-1 revealed numerical improvements despite missing the primary SRI(4) endpoint for SLE. Filing expected H2:20. We have modest sales estimates in our last published model pending visibility on the regulatory path.

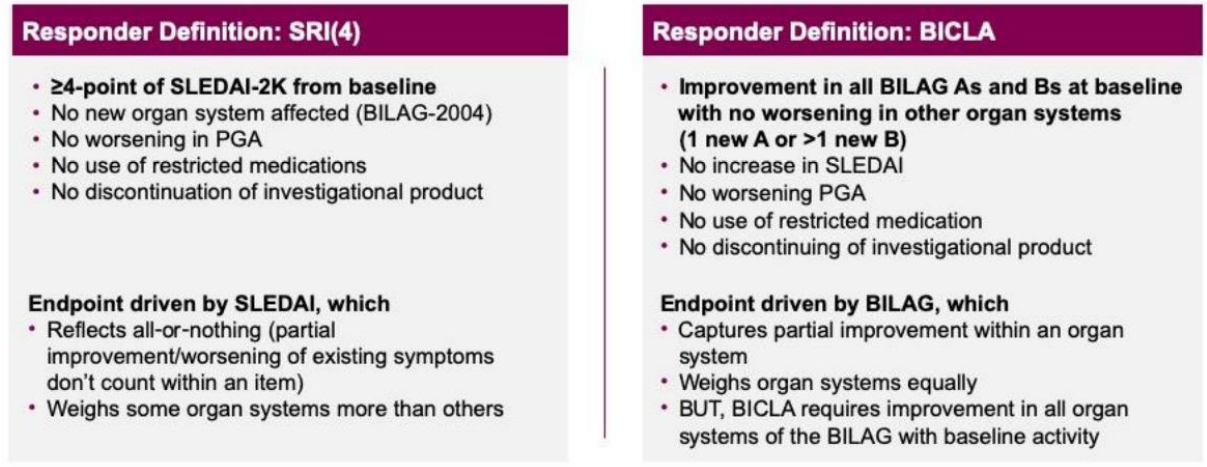
TULIP-1: Phase III study of 457 systemic lupus erythematosus (SLE) patients randomized 2:1:2 to receive anifrolumab (Type I Interferon Receptor inhibitor; 150 or 300 mg) or placebo with a primary composite endpoint of SRI(4) at 52 weeks. The trial did not meet its primary endpoint with SRI(4) response rates of 36.2% vs 40.4% for anifrolumab (300 mg) vs. placebo. In patients with high IFN gene signatures (IFNGS-high), SRI(4) response rates were 35.9% vs. 39.3%, respectively. Anifrolumab did improve skin-related disease as measured by >= 50% reduction in CLASI activity in 41.9% vs. 24.9% of patients on placebo (nominal p=0.05). Joint disease was also

improved with anifrolumab as measured by >= 50% reduction in active joints relative to placebo (47.0% vs. 32.3%). BICLA response rates, an alternative composite endpoint, were 37.1% in the anifrolumab group vs. 27.0% in the placebo group at week 52. Sustained oral steroid reduction in weeks 40 to 52 was achieved in 41.0% vs. 32.1% of anifrolumab vs. placebo-treated patients. In this analysis, it was discovered that ~8% of patients had been inappropriately misclassified as non-responders due to NSAID use unrelated to SLE disease. A post-hoc analysis was performed reincorporating these patients. All endpoints including SRI(4) favored anifrolumab benefit in this post-hoc analysis. Amended BICLA response rates increased to 46.1% for anifrolumab vs. 29.6% for placebo. A manageable increase in Herpes zoster infection rates was the most common adverse effect, occurring in 5.6%, 5.4%, and 1.6% of the anifrolumab 300 mg, 150 mg, and placebo dose groups, respectively.

TULIP-2: Phase III study of 362 SLE patients randomized 1:1 to receive anifrolumab (300 mg) or placebo with a primary composite endpoint of BICLA at 52 weeks. The trial met its primary endpoint with BICLA response rates of 47.8% vs. 31.5% for anifrolumab vs. placebo (p=0.0013). In IFNGS-high patients, BICLA response rates were 48.0% vs. 30.7%, respectively (p=0.0022). Anifrolumab improved CLASI response rates at week 12 (49.0% vs. 25.0% for placebo, p=0.0392). Joint count response was numerically improved with anifrolumab relative to placebo (42.2% vs. 37.5%) but did not reach statistical significance. Sustained oral steroid reduction was achieved in 51.5% vs. 30.2% of anifrolumab vs. placebo-treated patients. An exploratory analysis of SRI(4) showed response rates of 55.5% for the anifrolumab group vs. 37.3% for the placebo group (p<0.001). Herpes zoster infection rates were 7.2% in the anifrolumab group vs. 1.1% in the placebo group.

Our Take: These data make a compelling case for anifrolumab benefit in SLE, but do not satisfy the FDA requirement for two positive Ph III trials. Trial investigators suggest that discordance between TULIP-1 and TULIP-2 may reveal more about the subjectivity of the composite endpoints, particularly in rating joint disease, than it does about the drug. Differences in the SRI(4) vs. BICLA are outlined in a slide from the AZN presentation below. Whether regulators will be satisfied by the "totality of the data", however, is difficult to predict. If anifrolumab does ultimately earn approval, its safety/efficacy profile appears competitive with the only other approved SLE biologic, GSK's Benlysta. Benlysta has experienced slow growth since its 2011 approval, but superior efficacy and the addition of another treatment option could spur more rapid uptake of anifrolumab. Anifrolumab efficacy is also mediated by a different mechanism which is directly implicated in SLE pathophysiology. A BICLA response rate improvement of 17.3% over placebo in TULIP-2 places anifrolumab efficacy at the high end of KOL expectations. Anifrolumab appears to be particularly effective in skin disease (affecting ~80% of SLE patients) as well as IFNGS-high (60-80% of SLE patients). Separation between anifrolumab and placebo occurred as early as 4 weeks for BICLA and 8 weeks for CLASI, a potential advantage over Benlysta. Anifrolumab responses were also durable, and sustained steroid reduction is a benefit that physicians would eagerly welcome.

SRI vs BICLA Composite Disease Activity Measures



Source: AZN ACR Investor Call November 2019

Gastrointestinal

Nexium Pressured By Generics; EU Rights Out-Licensed

AstraZeneca had led the peptic ulcer market with its Nexium/Prilosec proton pump inhibitor (PPI) franchise. However, generics launched in February 2015 and are available in most major markets except for Japan, where the patent expires on 7/20/20. In December 2018, Astra licensed Nexium's European rights to Grunenthal for $700MM upfront and potential future milestones of $90MM. We estimate Nexium sales of $1.445B (-15%) in 2019, $1.3B in 2020, and $1.025B in 2025.

OTC Nexium Launched By Pfizer

In August 2012, Astra sold WW Nexium OTC rights to Pfizer for an upfront payment of $250MM. Sales of Nexium OTC triggered a contingent payment from Astra to Merck in 2014 (amount not disclosed). Nexium OTC is now marketed. Astra is eligible to receive milestone and royalty payments based on Nexium OTC launches and sales (details not disclosed), although royalty payments are not expected to contribute significantly to Astra revenue over time.

Infectious Diseases

FluMist Back On U.S. Market

FluMist, an intranasal influenza vaccine approved for use in healthy individuals aged 5 to 49, has not been able to compete effectively with the injectable vaccine. However, the second-generation benefits from a broader label for individuals aged 2 through 49 years (approved September 2007), and data showing it is more effective than traditional injectable vaccine. In February 2011, Fluenz (EU name) was granted EU approval for children 24 months to less than 18 years of age. FluMist Quadrivalent was approved in the U.S. in February 2012 and in the EU in December 2013. In September 2015, Astra licensed FluMist Quadrivalent to Daiichi Sankyo for development and commercialization in Japan. Astra will receive an upfront payment, development milestones, and

unspecified royalty payments on sales. Phase III studies have been conducted and a regulatory filing in Japan is being prepared.

In June 2016, the CDC announced its recommendation that FluMist Quadrivalent should not be used in the U.S. for the 2016-17 influenza season as testing demonstrated effectiveness of 46-58% for the 2015-16 vaccine, below the 50-60% level the CDC considers effective. These effectiveness results contrasted with Astra findings; the company worked with the CDC to better understand their data and prevent future discrepancies. In June 2017, ACIP again recommended against FluMist for the 2017-18 flu season. However, in mid-2018, CDC recommended that FluMist be allowed to re-enter the U.S. market for the 2018-19 flu season. U.S. FluMist Quadrivalent sales were $206MM in 2015, $33MM in 2016 (total sales of $104MM), and zero in 2017 (total sales of $78MM). We peg WW FluMist sales at $105MM (-5%) in 2019, $180MM in 2020, and $355MM in 2025.

Synagis U.S. Rights Out-Licensed

Synagis is a humanized monoclonal antibody for the prevention of lower respiratory tract disease resulting from respiratory syncytial virus (RSV) in pediatric patients. RSV is the leading cause of respiratory tract infections in infants and young children. It is estimated that more than 125,000 infants/children are hospitalized each year due to RSV infection. Synagis was launched in 1998 and has almost fully penetrated the less-than-32 weeks and greater-than-32 weeks' high-risk segments. Penetration into the 250K 32-35-week cohort has remained elusive, as there is tenuous medical need and lack of pharmacoeconomic data in this group. Guidelines from the American Academy of Pediatrics (AAP) issued in July 2014 recommended reducing the number of preterm infants who qualify for Synagis prophylaxis to those born at less than 29 weeks, down from the prior 32-week guidance. Other modest restrictions were also recommended. An October 2017 review by AAP upheld these recommendations.

In January 2019, Astra out-licensed the U.S. rights for Synagis to SOBI (Swedish Orphan Biovitrum) for $1.5B upfront ($1B cash, $500MM Sobi equity or ~8% ownership) and potentially up to $470MM in sales-related payments. SOBI also gains the right to participate in Astra's share of U.S. profits from MEDI8897 (single dose anti-RSV mAb being developed with Sanofi). We forecast Synagis sales of $385MM (-42%) in 2019, $280MM in 2020, and $180MM in 2025.

Nirsevimab RSV mAb In Phase II With Sanofi

In March 2017, Astra announced a collaboration with Sanofi to develop and commercialize nirsevimab (MEDI8897/SP0232), a mAb that neutralizes RSV (respiratory syncytial virus). RSV is the most common cause of respiratory tract infections in children under 1 y.o. It is formulated with a long-half-life such that only one dose is needed for the RSV season. Data from a Phase Ib/IIa study indicated a half-life of approximately 70 days which supports single dose administration.

In early Phase IIb data, MEDI8897 serum half-life ranged from 62.5-72.9 days. On day 151, 87% of infants receiving 50 mg had serum concentrations >90% effective concentration target level of 6.8 µg/mL, and 90% showed a ≥4-fold rise from baseline in serum RSV-neutralizing antibody levels. AEs were reported in 93.0% of MEDI8897 recipients vs. 94.4% on placebo; 3 MEDI8897 recipients experienced 5 serious AEs (3 LRTIs, 2 febrile seizures). Five MEDI8897 recipients experienced medically attended LRTIs through day 150; 1 tested positive for RSV (10 mg group).

Nirsevimab received Fast Track Designation in the U.S. in 2015; and received Breakthrough Therapy designation in the U.S. and PRIME designation in the EU in February 2019. Two Phase III studies are expected to initiate in July 2019: 1) Prevention of RSV lower respiratory tract infection in high-risk children (primary completion December 2021); and 2) Prevention of RSV lower respiratory tract infection in healthy late pre-term and term Infants (primary completion May 2022). Submission is planned for 2023. Pricing will likely be vaccine-like (although not flu vaccine-like) in order to extend the reach of the drug. However, benchmarking against the cost of hospitalization works in favor of nirsevimab's pharmacoeconomics. Sanofi paid AZN €120MM upfront and may pay up to €495MM in milestones. The companies will share all costs and profits. Astra will lead development to first approval; Sanofi will lead commercialization. We estimate sales for nirsevimab of $25MM in 2024 and $50MM in 2025.

As part of the September 2019 transaction with SOBI for Synagis, SOBI also gained the right to participate in Astra's share of profits and losses related to nirsevimab.

AstraZeneca 2019-25 Balance Sheet Analysis ($MM)

	2018A	2019E	2020E	2021P	2022P	2023P	2024P	2025P
Assets								
Cash & Equivalents	$4,831	$4,670	$5,125	$5,025	$7,240	$10,740	$15,115	$21,125
Inventories	2,890	3,160	3,455	3,895	4,245	4,565	4,910	5,245
Accounts Receivable	5,574	5,350	5,845	6,660	7,360	7,980	8,705	9,360
Other Current Assets	2,296	1,200	1,200	1,200	1,200	1,200	1,200	1,200
Total Current Assets	**$15,591**	**$14,380**	**$15,625**	**$16,780**	**$20,045**	**$24,485**	**$29,930**	**$36,930**
Property, Plant & Equipment	$7,421	$7,300	$7,325	$7,350	$7,375	$7,400	$7,425	$7,450
Goodwill	11,707	11,500	11,450	11,400	11,350	11,300	11,250	11,200
Intangible Assets	21,959	21,000	20,900	20,800	20,700	20,600	20,500	20,400
Deferred Tax Assets	2,379	2,500	2,500	2,500	2,500	2,500	2,500	2,500
Other Long-Term Assets	1,594	2,500	2,500	2,500	2,500	2,500	2,500	2,500
Total Long-Term Assets	**$45,060**	**$44,800**	**$44,675**	**$44,550**	**$44,425**	**$44,300**	**$44,175**	**$44,050**
Total Assets	**$60,651**	**$59,180**	**$60,300**	**$61,330**	**$64,470**	**$68,785**	**$74,105**	**$80,980**
Liabilities								
Short-Term Debt	$1,754	$500	$500	$500	$500	$500	$500	$500
Accounts & Other Payable	12,841	12,675	13,395	14,670	15,560	16,255	17,080	17,815
Current Income Tax Liabilities	1,164	1,100	1,100	1,100	1,100	1,100	1,100	1,100
Provisions/Contingent and Other	533	500	500	500	500	500	500	500
Total Current Liabilities	**$16,292**	**$14,775**	**$15,495**	**$16,770**	**$17,660**	**$18,355**	**$19,180**	**$19,915**
Long-Term Debt	$17,359	$17,000	$16,500	$16,000	$15,500	$15,000	$14,500	$14,000
Deferred Tax Liabilities	3,286	2,900	2,900	2,900	2,900	2,900	2,900	2,900
Other Long-Term Liabilities	9,670	10,000	10,000	10,000	10,000	10,000	10,000	10,000
Total Long-Term Liabilities	**$30,315**	**$29,900**	**$29,400**	**$28,900**	**$28,400**	**$27,900**	**$27,400**	**$26,900**
Total Liabilities	**$46,607**	**$44,675**	**$44,895**	**$45,670**	**$46,060**	**$46,255**	**$46,580**	**$46,815**
Net Equity	**$14,044**	**$14,505**	**$15,405**	**$15,660**	**$18,410**	**$22,530**	**$27,525**	**$34,165**

Company reports; Cowen and Company estimates

AstraZeneca 2019-25 Working Capital Analysis ($MM)

	2018A	2019E	2020E	2021P	2022P	2023P	2024P	2025P
Inventories	$2,890	$3,160	$3,455	$3,895	$4,245	$4,565	$4,910	$5,245
COGS	4,319	4,721	5,160	5,820	6,345	6,820	7,335	7,835
Inventory Turns	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Months	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
Accounts Receivable	$5,574	$5,350	$5,845	$6,660	$7,360	$7,980	$8,705	$9,360
Sales	22,090	24,405	26,735	30,395	33,575	36,410	39,715	42,715
Receivables Days	92	80	80	80	80	80	80	80
Accounts Payable	$12,841	$12,675	$13,395	$14,670	$15,560	$16,255	$17,080	$17,815
COGS	$4,319	$4,721	$5,160	$5,820	$6,345	$6,820	$7,335	$7,835
Payables Days	1085	980	950	920	895	870	850	830
Net Working Capital (Ex. Cash, Debt)	($4,377)	($4,165)	($4,095)	($4,115)	($3,955)	($3,710)	($3,465)	($3,210)

Source: Company reports; Cowen and Company estimates

AstraZeneca 2019-25 Cash Flow Analysis ($MM)

	2018A	2019E	2020E	2021P	2022P	2023P	2024P	2025P
Operating Activities								
Pretax Income (adjusted)	$4,822	$5,831	$6,660	$8,300	$9,855	$11,405	$13,130	$14,945
Depreciation & Amort.	3,753	3,700	3,725	3,750	3,775	3,800	3,825	3,850
Change in Working Capital	780	(212)	(70)	20	(160)	(245)	(245)	(255)
Restruct/Acquis/Divest related costs	(2,659)	(2,500)	(2,000)	(2,000)	(2,000)	(2,000)	(2,000)	(2,000)
Income Taxes Paid	(537)	(900)	(950)	(975)	(1,000)	(1,025)	(1,050)	(1,075)
Other, net	(3,541)	(2,500)	(1,500)	(1,500)	(1,500)	(2,000)	(2,000)	(2,000)
Net Cash From Operations	**$2,618**	**$3,419**	**$5,865**	**$7,595**	**$8,970**	**$9,935**	**$11,660**	**$13,465**
Investing Activities								
Capital Expenditures Net	($1,031)	($1,025)	($1,050)	($1,075)	($1,100)	($1,125)	($1,150)	($1,175)
Acquisitions/Combinations/Sales -net	1,396	(1,300)	(675)	0	0	0	0	0
Purchase/sale financial instruments	598	0	0	0	0	0	0	0
Other, net	0	0	0	0	0	0	0	0
Net Cash From Investing	**$963**	**($2,325)**	**($1,725)**	**($1,075)**	**($1,100)**	**($1,125)**	**($1,150)**	**($1,175)**
Financing Activities								
Debt Financings - net	$1,571	($500)	($500)	($500)	($500)	($500)	($500)	($500)
Dividend Payments	(3,484)	(3,640)	(3,740)	(3,805)	(3,870)	(3,935)	(4,000)	(4,000)
Share Repurchase	34	3,500	0	0	0	0	0	0
Other, net	(165)	0	0	0	0	0	0	0
Net Cash From Financing	**($2,044)**	**($640)**	**($4,240)**	**($4,305)**	**($4,370)**	**($4,435)**	**($4,500)**	**($4,500)**
Fx Adjustment	($38)							
Net Change in Cash & Equivalents	$1,499	$454	($100)	$2,215	$3,500	$4,375	$6,010	$7,790
Year-End Cash & Equivalents	**$4,671**	**$5,125**	**$5,025**	**$7,240**	**$10,740**	**$15,115**	**$21,125**	**$28,915**

Source: Company reports; Cowen and Company estimates

AZN DCF Analysis

Assumptions		*Output*	
		Equity Value	$142,391
		Estimated Share Price	$55
Discount Rate	8.1%	Net Cash	($14,282)
Shares Outstanding	1,301	Enterprise Value	$156,673

AZN DCF

	2018A	2019E	2020E	2021P	2022P	2023P	2024P	2025P	2026P	2027P	2028P	2029P	2030P	Terminal
Total Revenues	$22,090	$24,405	$26,735	$30,395	$33,575	$36,410	$39,715	$42,715	$45,705	$48,447	$50,870	$52,905	$55,021	
% Change	-2%	+10%	+10%	+14%	+10%	+8%	+9%	+8%	+7%	+6%	+5%	+4%	+4%	
Cost of Goods	$4,650	$5,061	$5,510	$6,180	$6,715	$7,205	$7,735	$8,250	$8,912	$9,447	$9,920	$10,316	$10,729	
Gross Profit	$17,441	$19,344	$21,225	$24,215	$26,860	$29,205	$31,980	$34,465	$36,793	$39,000	$40,950	$42,588	$44,292	
Gross Margin - Total	79.0%	79.3%	79.4%	79.7%	80.0%	80.2%	80.5%	80.7%	80.5%	80.5%	80.5%	80.5%	80.5%	
SG&A	$8,651	$8,740	$9,160	$10,075	$10,770	$11,270	$12,025	$12,400	$13,254	$14,050	$14,752	$15,342	$15,956	
% of Revs	39.2%	35.8%	34.3%	33.1%	32.1%	31.0%	30.3%	29.0%	29.0%	29.0%	29.0%	29.0%	29.0%	
R&D	$5,266	$5,290	$5,495	$5,910	$6,250	$6,500	$6,750	$7,000	$7,541	$7,994	$8,394	$8,994	$9,354	
% of Revs	23.8%	21.7%	20.6%	19.4%	18.6%	17.9%	17.0%	16.4%	16.5%	16.5%	16.5%	17.0%	17.0%	
Operating Expenses	$13,917	$14,030	$14,655	$15,985	$17,020	$17,770	$18,775	$19,400	$20,796	$22,044	$23,146	$24,336	$25,310	
% of Revenues	63.0%	57.5%	54.8%	52.6%	50.7%	48.8%	47.3%	45.4%	45.5%	45.5%	45.5%	46.0%	46.0%	
Other operating income	$2,147	$1,410	$900	$800	$700	$600	$500	$400	$300	$200	$100	$50	$0	
Operating Income	$5,681	$6,724	$7,470	$9,030	$10,540	$12,035	$13,705	$15,465	$16,297	$17,157	$17,904	$18,302	$18,982	
% Operating Margin	25.7%	27.6%	27.9%	29.7%	31.4%	33.1%	34.5%	36.2%	35.7%	35.4%	35.2%	34.6%	34.5%	
EBIT	$5,681	$6,724	$7,470	$9,030	$10,540	$12,035	$13,705	$15,465	$16,297	$17,157	$17,904	$18,302	$18,982	
% of Revs	25.7%	27.6%	27.9%	29.7%	31.4%	33.1%	34.5%	36.2%	35.7%	35.4%	35.2%	34.6%	34.5%	
D&A	$3,753	$3,700	$3,725	$3,750	$3,775	$3,800	$3,825	$3,850	$3,870	$3,890	$3,910	$3,930	$3,950	
EBITDA	$9,434	$10,424	$11,195	$12,780	$14,315	$15,835	$17,530	$19,315	$20,167	$21,047	$21,814	$22,232	$22,932	
% of Revs	42.7%	42.7%	41.9%	42.0%	42.6%	43.5%	44.1%	45.2%	44.1%	43.4%	42.9%	42.0%	41.7%	
Net Interest Income (Expense)	($736)	($763)	($670)	($600)	($550)	($490)	($430)	($370)	($350)	($345)	($340)	($335)	($330)	
Joint Ventures	($113)	($120)	($125)	($130)	($135)	($140)	($145)	($150)	($155)	($160)	($165)	($170)	($175)	
Pre-Tax Income	$4,832	$5,841	$6,675	$8,300	$9,855	$11,405	$13,130	$14,945	$15,792	$16,652	$17,399	$17,797	$18,477	
Taxes	$549	$1,193	$1,332	$1,660	$1,971	$2,281	$2,626	$2,989	$3,158	$3,330	$3,480	$3,559	$3,695	
Income Tax Rate	11.4%	20.4%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	
Net Income	$4,384	$4,708	$5,403	$6,700	$7,944	$9,184	$10,564	$12,016	$12,693	$13,381	$13,980	$14,298	$14,842	
% of Revs	19.8%	19.3%	20.2%	22.0%	23.7%	25.2%	26.6%	28.1%	27.8%	27.6%	27.5%	27.0%	27.0%	
NOPAT	$5,132	$5,531	$6,138	$7,370	$8,569	$9,754	$11,079	$12,476	$13,138	$13,826	$14,425	$14,743	$15,287	
Adjustments:														
Capex	($1,031)	($1,025)	($1,050)	($1,075)	($1,100)	($1,125)	($1,150)	($1,175)	($1,200)	($1,225)	($1,250)	($1,275)	($1,300)	
Depreciation & Amortization	$3,753	$3,700	$3,725	$3,750	$3,775	$3,800	$3,825	$3,850	$3,870	$3,890	$3,910	$3,930	$3,950	
Change In Working Capital	$780	($212)	($70)	$20	($160)	($245)	($245)	($255)	($200)	($200)	($200)	($200)	($200)	
Operating Free Cash Flow	$7,886	$7,171	$8,008	$9,395	$10,459	$11,614	$12,994	$14,436	$15,163	$15,846	$16,440	$16,753	$17,292	$195,633

Source: Company data, Cowen and Company

AstraZeneca R&D Pipeline

Therapeutic Class/Product	PC	I	II	III	NDA Filed	Expected Filing	Comments
Analgesia/Anesthesia							
MEDI-7352			•				NGF/TNF bi-specific Mab; osteoarthritis pain
Cancer/Oncology/Hematology							
Lynparza		•	•	•		2020+	Olaparib; oral PARP inhibitor; approved in breast and ovarian cancers; filed in China for gBRCA metastatic breast cancer (OLYMPIAD); filed in US pancreatic cancer (positive AdComm Dec-19); PIII prostate (Breakthrough Therapy); various PI/II combinations; w/ MRK
Tagrisso		•	•	•		2020+	AZD 9291; approved for 1L/2L EGFR NSCLC; PIII for Stage III unresectable NSCLC, adjuvant NSCLC; PII and PI combos for EGFRm NSCLC
Calquence		•	•	•	2019		Acalabrutinib; BTK inhibitor; approved for MCL, CLL; PIII for r/r MCL; PII/III for lymphocytic leukemia, PI/II various solid tumors
Imfinzi		•	•	•		2020+	Durvalumab; anti-PD-L1 mAb; approved 2018 in U.S./EU for Stage III unresected NSCLC; PIII 1L SCCHN, 1L HCC, SCLC, NSCLC, other cancers; PII solid tumors; PII/PIII 1L SCLC, collaborations and combinations for multiple indications; multiple PI combos
Savolitinib			•	•		2020+	AZD 6094; cMET inhibitor; SAVOIR PIII trial initiated Jun-17; papillary renal cell carcinoma; PII in combo with Targrisso NSCLC
Selumetinib		•	•	•		2020+	AZD 6244; MEK inhibitor; PIII (registrational) pedi neurofibromatosis; PII ALL, NF1 tumors, peripheral nerve sheath tumors, combo with Tagrisso for NSCLC, PI combo with durvalumab for solid tumors; with MRK
Trastuzumab deruxtecan			•	•	2019		DS-8201; ADC targeting HER2; approved U.S., field JP for HER2+ BC; PIII Breast, HER2-low BC, GI; PII CRC, NSCLC
Tremelimumab		•	•	•		2020	Anti-CTLA4; PIII combo with durvalumab in 1L NSCLC, SCLC, bladder; PII combo with durvalumab, gastric cancer; various PI/PII combinations for solid tumors
Capivasertib			•	•			AZD 5363; AKT kinase inhibitor; positive Phase II data presented ASCO '19 in TNBC; PIII breast, prostate
Monalizumab			•	•			NKG2a mAb; Inhibitory cell surface receptor covalently bound to CD94; PIII H&N cancer; PII H&N, CRC, ovarian, CLL

AstraZeneca R&D Pipeline

Therapeutic Class/Product	PC	I	II	III	NDA Filed	Expected Filing	Comments
Adavosertib		•	•				AZD 1775; WEE-1 inhibitor; monotherapy and combos with Lynparza and durvalumab for solid tumors, with chemo for ovarian cancer; PII ovarian, breast, gastric, SCLC; PI solid tumors
AZD 2811			•				Aurora B kinase inhibitor; solid tumors, 2L SCLC; with Bind Therapeutics
AZD 4635		•	•				A2aR inhibitor; PI combo w/oleclumab for EGFRm NSCLC; PII solid tumors; with Heptares Therapeutics
AZD 5069			•				CXCR2; PII in combo with Imfinzi HNSCC
AZD 6738		•	•				Ceralasertib; ATR serine / threonine kinase inhibitor; PII solid tumors, combo w/ Lynparza for gastric, breast; PI combo w/ Calquence for hematological malignancies
MEDI-0457		•	•				INO-3112; HPV vaccine; PI and PII in HPV-related cancers; alone and in combination with Durvalumab; w/ Inovio
Oleclumab		•	•				MEDI-9447; CD73 mAb; PII combo with durvalumab for NSCLC, pancreatic, solid tumors; PI monotherapy solid tumors, combo w/ AZD4635 or Targrisso in EGFRm NSCLC
AZD 1390		•					ATM inhibitor; glioblastoma
AZD 4573		•					CDK9 inhibitor; hematological malignancies
AZD 5153		•					BRD4 inhibitor; solid tumors
AZD 5991		•					MCL1 inhibitor; hematological malignancies
AZD 9496		•					Selective estrogen receptor downregulator (SERD); ER+ breast cancer
AZD 9833		•					Selective estrogen receptor downregulator (SERD); PI mono and in combo with palbociclib in women with ER+, HER2- advanced BC
MEDI-2228		•					BCMA ADC; multiple myeloma
MEDI-3726		•					PSMA antibody drug conjugate; prostate cancer
MEDI-5083		•					Immune activator; solid tumors
MEDI-5752		•					PD-1/CTLA4 bispecific mAb; solid tumors
MEDI-7247		•					ADC; hematological malignancies
MEDI-1191		•					IL-12 mRNA for solid tumors
AZD 0466		•					Bcl2/xL inhibitor with DEP delivery; w/ Starpharma
Cardiovascular							
Lokelma				•	•	2020	Potassium binder; hyperkalaemia; approved U.S, EU; in development in China, JP; filing H2:2019 in JP, 2020 in China
Epanova				•		2020+	Omega-3 carboxyic acids; approved in U.S.; STRENGTH outcomes trial in statin-treated patients at high CV risk with persistent hypertriglyceridemia + low HDL

AstraZeneca R&D Pipeline

Therapeutic Class/Product	PC	I	II	III	NDA Filed	Expected Filing	Comments
Brilinta				•	2019	2020+	Reversible ADP receptor antagonist; filed in U.S. and EU based on THEMIS outcomes study in T2DM and CAD (positive topline Feb 2019); HESTIA study in sickle cell; THALES in stroke
AZD 4831			•				Myeloeroxidase; heart failure with a preserved ejection fraction
AZD 8601			•				VEGF-A; cardiovascular
AZD-5718			•				5-lipoxygenase-activating protein (FLAP); coronary artery disease
MEDI-5884			•				Cholesterol modulation; PII ACS, stable coronary heart disease
MEDI-6012			•				LCAT; acute coronary syndrome
AZD 8233		•					Hypercholestrolemia
AZD 9977		•					Mineralocorticoid receptor modulator; CV disease
MEDI-6570		•					LOX-1 mAb; cardiovascular disease
AZD6615		•					Hypercholesterolemia
Central Nervous System							
MEDI-1341		•					Alpha synuclein mAb; Parkinson's
MEDI-1814		•					AB42 Mab; amyloid beta; Alzheimer's disease; with LLY
Dermatologic							
AZD 0284		•					Inhaled RORg; psoriasis, respiratory
Diabetes							
Farxiga				•	2019		Dapagliflozin; SGLT2 inhibitor; approved for T1DM in EU (Mar-19) and JP (Mar-19), recieved CRL in U.S. (Jul-19); approved in U.S. for reduction of HF in T2DM and established CVD (Oct-19, based on DECLARE), also filed in EU (positive CHMP opinion Jul-19); Fast Track Designations for HF/CVOT and CKD
Bydureon				•			GLP-1 receptor agonist; T2DM; CV outcomes data under review U.S., EU
Xigduo				•		2020	SGLT-2 inhibitor/metformin FDC; T2 diabetes; launched in U.S. and EU; expected filing in China 2020
Cotadutide			•				MEDI-0382; GLP-1/glucagon dual agonist; diabetes/obesity; positive Phase Iia data showing improved glycemic control, weight loss presented Q2:18, PIIb data expected 2019
MEDI-7219		•					T2DM
Gastroenterology/Heptology							
Nexium			•	•	•		Proton pump inhibitor; stress ulcer prophylaxis; accepted in China; PIII Preeclampsia; PII GI erosions, children w/ Autism

AstraZeneca R&D Pipeline

Therapeutic Class/Product	PC	I	II	III	NDA Filed	Expected Filing	Comments
Cotadutide			•				GLP-1/glucagon coagonist; NASH; PII initiated Q3:19
Infectious Disease							
MEDI-3902			•				PsI/PcrV bispecific mAb; prevention of nosocomial Pseudomonas aeruginosa pneumonia; Fast Track status
Nirsevimab			•				MEDI-8897; Anti-RSV Mab-YTE; passive RSV prophylaxis; Fast Track designation Apr-15, Breakthrough Therapy designation Feb-19, EMA PRIME status Feb-19; w/ Sanofi, licensed to Sobi
Suvratoxumab			•				MEDI-4893; mAb binding to Staph aureus toxin; prevention of nosocomial S. aureus pneumonia; Fast Track status
Nephrology							
Roxadustat				•	•	2020+	Hypoxia-inducible factor inhibitor; anemia in CKD/ESRD; approved in China (Dec-18), JP (Sept-19) for dialysis patients; approved in China for non-dialysis patients (Q3:19); PIII EU; PIII anemia due to oncology treatment; PII Chemo-induced anemia
Verinurad			•				URAT inhibitor; chronic kidney disease
Respiratory							
Bevespi Aerosphere				•	•		PT003; LABA/LAMA; approved in U.S., EU Dec-18; under review China/Japan; PIII for COPD
Breztri Aerosphere			•	•	2018, 2019		PT010; LAMA/LABA/ICS, Pearl triple; approved for COPD in JP (Jun-19); filed for COPD in CN (2018), received CRL in U.S. (Q3:19), filed in EU; PIII COPD; PII asthma
Fasenra				•		2020+	Benralizumab; anti-IL-5R MAb; approved for severe asthma in U.S., EU; approved in U.S. for self-administration w/ pre-filled auto-injector, Oct-19; COPD trials failed; FDA Orphan Drug Designation for eosinophilic oesophagitis; PIII for severe uncontrolled asthma, nasal polyposis
PT027				•			ICS/SABA; asthma; PIII initiated H1:19
Tezepelumab			•	•		2020+	TSLP mAb; PIII asthma w/Amgen, PII atopic dermatitis, COPD
Abediterol			•				AZD 0548; LABA; asthma, COPD
AZD 7594			•				Inhaled SGRM; PII mono asthma/COPD
AZD 7986			•				DPP1; COPD
AZD 8871			•				MABA; COPD
AZD 9567			•				Oral SGRM; respiratory
AZD 0449		•					Inhaled JAK inhibitor; asthma
AZD 1402		•					Inhaled IL-4Ra; asthma
AZD 5634		•					Inhaled ENaC; cystic fibrosis
AZD 8154		•					Inhaled P13Kgd; asthma

AstraZeneca R&D Pipeline

Therapeutic Class/Product	PC	I	II	III	NDA Filed	Expected Filing	Comments
MEDI-3506		•					IL-33 mAb; COPD
Rheumatology/Inflammation/Immunology							
Anifrolumab			•	•		2020	MEDI-546; anti-IFNaR Mab; PIII SLE (Fast Track; 3 PIII trials), failed first PIII trial Aug'18; PIII TULIP 2 met primary endpoint (Q3:19); PII lupus nephritis
AZD 9567			•				Oral SGRM; rheumatoid arthritis
Total Drugs in Development	**0**	**27**	**25**	**22**	**3**		**75**

Markers counted towards column totals, if not advanced into further phases

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Source: Cowen and Company

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Ticker	Company Name
AZN	AstraZeneca PLC (ADR)

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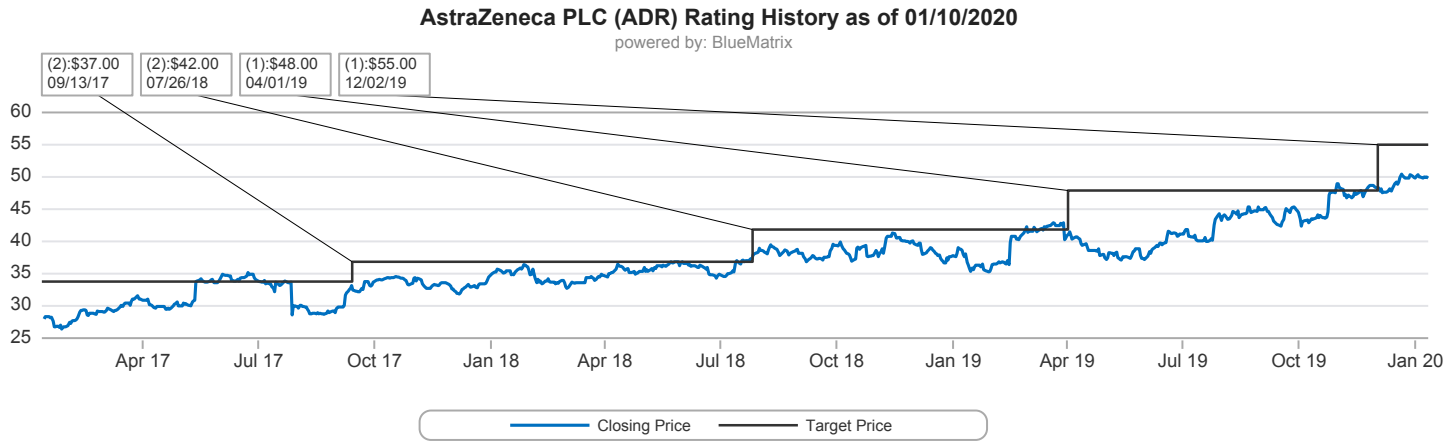

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