

The logo for CHI-MED, featuring the letters 'CHI-' in white on a red rounded rectangular background.

CHI-

The logo for MED, featuring the letters 'MED' in black on a white rounded rectangular background with a black border.

MED

HUTCHISON CHINA MEDITECH

2018 Interim Results

AIM/Nasdaq: HCM

July 27, 2018

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The performance and results of operations of the Chi-Med Group contained within this presentation are historical in nature, and past performance is no guarantee of future results.

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*Use of Non-GAAP Financial Measures* - Certain financial measures used in this presentation are based on non-GAAP financial measures. Please see the appendix slides titled "Non-GAAP Financial Measures and Reconciliation" for further information relevant to the interpretation of these financial measures and reconciliations of these financial measures to the most comparable GAAP measures.

# Latest Updates

*H1 2018 - Financial and Operational Highlights  
... aiming to get 3 novel drugs approved in next 3 years*

# Chi-Med Highlights

Momentum continues to build...



## Deep Pipeline Approaching Approvals

### NDA approval

Fruquintinib CRC & NSCLC

*CRC NDA process near end target launch H2 2018<sup>[1]</sup>*

*Target NSCLC top-lines H2 2018*

### Breakthrough

*4 global reg. studies planned for savolitinib*

*1L/2L PRCC 2L NSCLC  
2L/3L NSCLC 1L NSCLC<sup>[2]</sup>*

**10 more shots at approvals**

aiming for

**3 drugs approved in next 3 years**

**20+ Ph. Ib/II PoCs**

on 8 candidates

*Currently enrolling*

*Opened new U.S. office for global development*

## Prolific Discovery Engine

**Fully Integrated - Chemistry Depth**

~390 scientific team

**8 Clinical Candidates**

all discovered in-house

**2<sup>nd</sup>-gen IO INDs**

every 1~2 years

## Established Commercial Organization

**Pan-China Sales & Marketing**

~2,400 medical reps

**Product Launch Ready**

proven success in new indications

[1] Subject to China National Drug Administration approval; [2] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients; mCRC = metastatic colorectal cancer; PRCC = papillary renal cell carcinoma; NSCLC = non-small cell lung cancer; PoC = Phase Ib/II proof-of-concept study; IO = immuno-oncology; IND = Investigational New Drug.

# H1 2018 Financial Results

Including **\$66.7 million** in innovation investment <sup>[1]</sup><sup>[2]</sup>

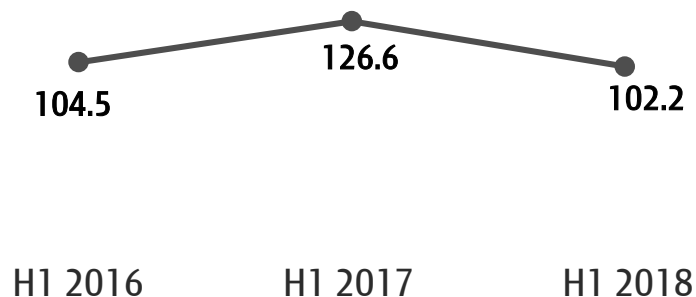


## Financial Summary

	H1- 2016	H1- 2017	H1- 2018	Change	
				16-17	17-18
<b>REVENUES</b>	104.5	126.6	102.2	21%	-19%
<i>Unconsolidated JV Revenues</i> <sup>[3]</sup>	227.5	224.2	271.7	-1%	21%
<b>NET INCOME/(LOSS)</b> <sup>[2]</sup>					
<b>INNOVATION PLATFORM</b>	(13.7)	(14.8)	(52.9)	-8%	-258%
<i>Base HMP Operations</i>	(11.6)	(12.4)	(50.5)		
<i>50% share of Nestle JV (NSP)</i> <sup>[4]</sup>	(2.1)	(2.4)	(2.4)		
<b>COMMERCIAL PLATFORM</b>	22.1	22.7	26.9	2%	19%
<i>Prescription Drugs Business</i>	15.3	16.9	20.8		
<i>Consumer Health Business</i>	6.8	5.8	6.1		
<b>Chi-Med Group Costs</b>	(7.9)	(8.7)	(6.7)	-10%	23%
<i>General &amp; Administrative Expenses</i>	(5.8)	(6.6)	(4.9)		
<i>Interest/Tax</i>	(2.1)	(2.1)	(1.8)		
<b>R&amp;D Related Subsidies</b>	-	2.5	-	100%	n/a
<b>Net Income/(Loss) Attrib. to Chi-Med</b>	0.5	1.7	(32.7)	213%	n/a
<i>EPS Attrib. to Ord. S-H (Basic) (US\$)</i>	0.01	0.03	(0.49)		

## Group Results

### Revenues



### Net Income/(Loss) <sup>[5]</sup>



[1] R&D expenses (Non-GAAP); H1 2017: \$37.5m; [2] GAAP R&D expenses were \$60.1m in H1 2018 (H1 2017: \$31.6m) - please see appendix "Non-GAAP Financial Measures and Reconciliation";

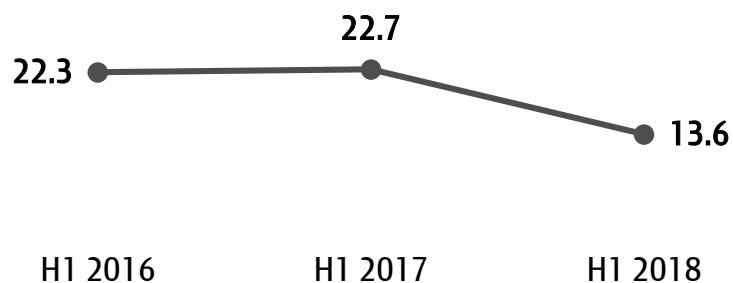
[3] Excluding Guanbao (divested); [4] NSP = Nutrition Science Partners Limited; [5] Net Income/(Loss) = Net Income/(Loss) Attributable to Chi-Med.

(US\$ millions,  
Except per share data)

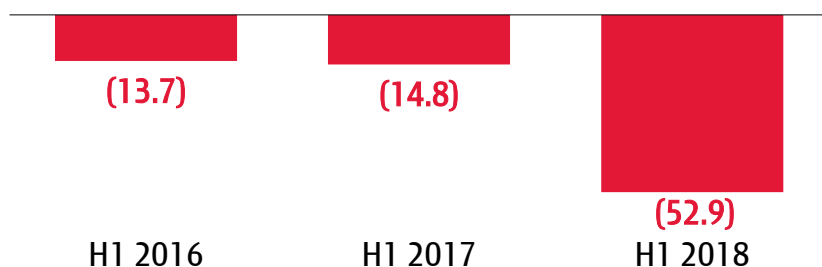
# Financial Performance of Main Platforms

## Innovation Platform

### Revenues



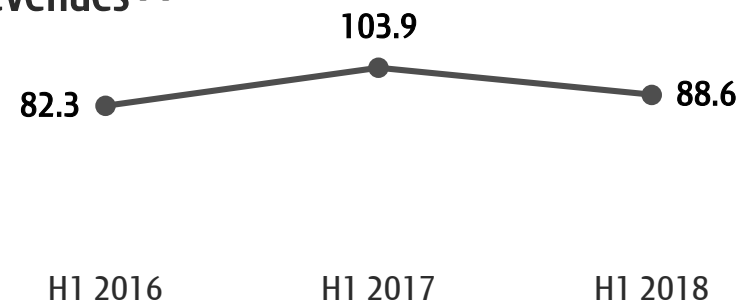
### Net Loss <sup>[3]</sup>



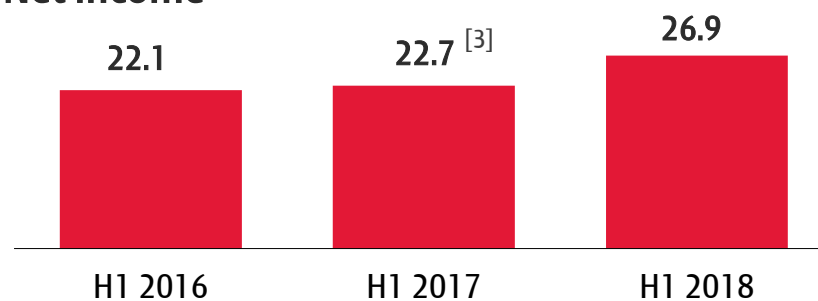
- No milestones in H1 2018, expected H2 2018;
- Increased R&D expense: **Acceleration in growth in operations & clinical trial activities.**

## Commercial Platform

### Revenues <sup>[1]</sup>



### Net Income <sup>[2]</sup>



- **China Two-Invoice System (TIS) implemented:** Move to fee-for-service model from revenue consolidation on some 3<sup>rd</sup> party drugs. **No effect on net income.**

[1] Only includes revenues of subsidiaries for Prescription Drugs and Consumer Health businesses - excludes joint ventures; [2] Adjusted Net Income/(Loss) = Adjusted Net Income/(Loss) attributable to Chi-Med (non-GAAP);

[3] Excludes the share of a one-time gain from SHPL's R&D related subsidies of US\$2.5 million.

# Summary Balance Sheet & 2018 Guidance

## Chi-Med Group-level Cash Position

as at Jun 30, 2018

- **\$416.9m available resources**  
(Dec 31, 2017: \$479.6m)
  - ✓ \$322.5m cash & cash equiv. and short-term investments <sup>[1]</sup>;
  - ✓ \$94.4m unutilized banking facilities <sup>[2]</sup> held.
- **\$26.7m in bank borrowings**  
(Dec 31, 2017: \$30.0m)
  - ✓ Weighted avg. cost of borrowing on outstanding loan 2.3%.

## Joint Venture-level Cash Position

as at Jun 30, 2018

- **\$62.5m available cash**  
(Dec 31, 2017: \$67.0m)
  - ✓ \$23.5m dividend to Chi-Med Group in H1 2018.

## 2018 Guidance

- **Innovation Platform: R&D expense up due to:**
  - ✓ **Share option grant** to middle management in Apr 2018;
  - ✓ **Inflation of clinical costs** - high activity in China biotech.
- **Commercial Platform: No change.**

	2017 Actual	2018 Guidance (March 12, 2018)	2018 Guidance (July 27, 2018)
<b>Revenues</b>	\$241.2	\$155 - \$175	\$155 - \$175
<b>Innovation Platform</b>			
Revenue	36.0	40 - 50	40 - 50
Adjusted R&D expenses (non-GAAP) <sup>[3]</sup>	(88.0)	(110) - (120)	(130) - (140)
<b>Commercial Platform</b>			
Sales (consolidated)	205.2	115 - 125	115 - 125
Sales of non-consolidated JVs	472.0	460 - 480	460 - 480
<b>Net Income</b>			
<i>On adjusted (non-GAAP) basis excluding one-time gains</i>	37.5	41 - 43	41 - 43
<i>One-time gains <sup>[4]</sup></i>	2.5	0 - 20	0 - 20
<b>Net Income</b>	40.0	41 - 63	41 - 63
<b>Chi-Med Group Costs</b>			
Admin., interest, tax	(14.8)	(16) - (18)	(16) - (18)
<b>Net Loss Attributable to Chi-Med</b>	(26.7)	(19) - (52)	(39) - (72)

[1] Short-term investments: 91-183 days deposits; [2] From Scotiabank, Bank of America Merrill Lynch, Deutsche Bank, Hong Kong Shanghai Banking Corporation; [3] R&D expenses, as adjusted (non-GAAP) excludes the actual or estimated impact of the revenue received from external customers of our Innovation Platform, which is reinvested into our clinical trials; [4] Share of potential land compensation from HBYS Plot 2 in 2018 guidance (dependent on Guangzhou government policy).

A composite background image. The top left shows a close-up of a person in a white lab coat using a pipette to transfer liquid into a multi-well plate. The top right shows a person's hand pointing at a whiteboard with blue chemical structures drawn on it. The bottom half of the image is a white banner containing text.

# Updates on Key Clinical Programs

*Chi-Med's most advanced assets*





# 11 shots at approvals

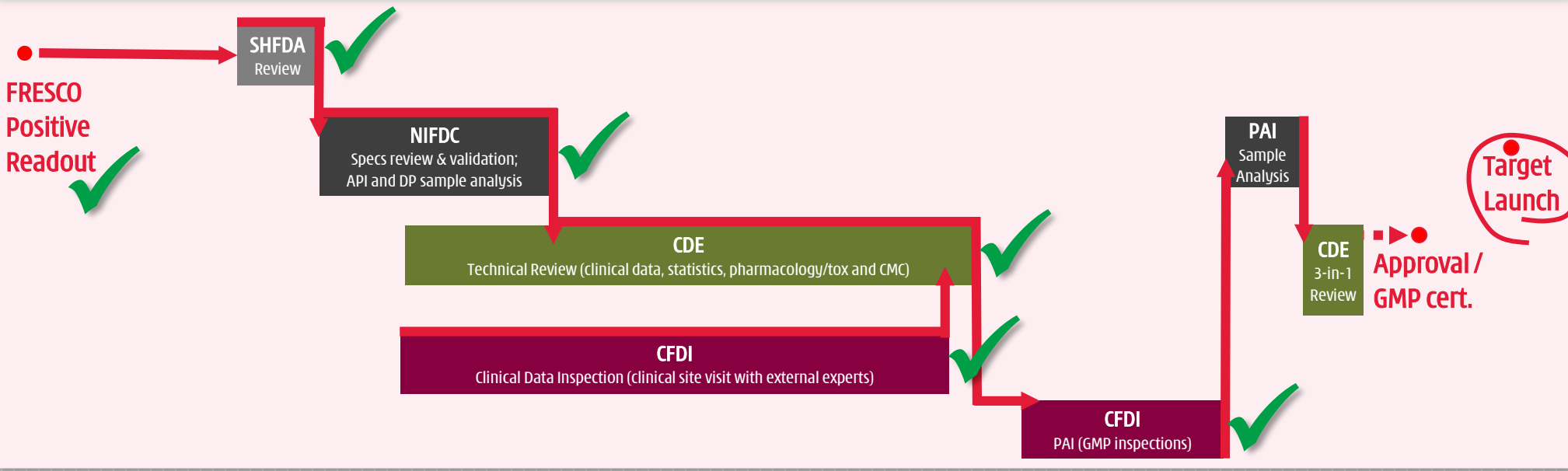
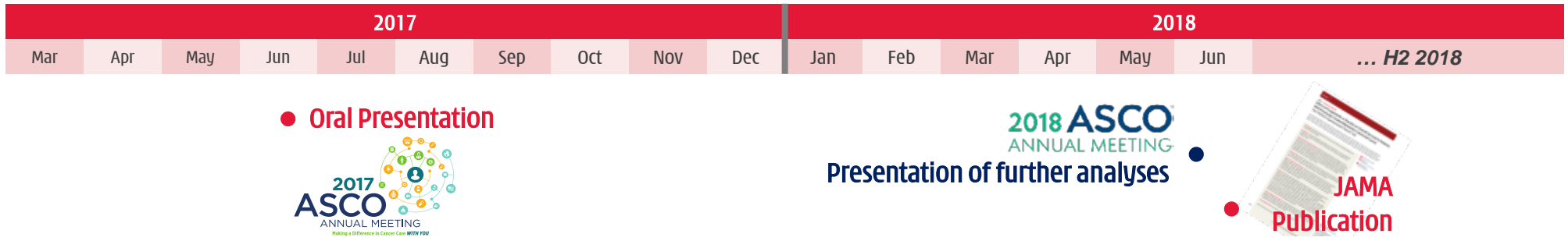
...aiming to get 3 novel drugs approved in next 3 years



					Breakthrough Therapy Potential	Registration Study Results Expected
SAVO	Papillary renal cell carcinoma (MET-driven)	Pivotal Phase III	Global	Enrolling	Molecular epidemiology study MET as -ve prognostic H2 2018	2020
	NSCLC -2L 1 <sup>st</sup> Gen EGFR TKI refract, Tagrisso combo (MET+, T790M+/-)	Pivotal Phase II/III [1]	Global	Controlled study to initiate in H1 2019 [2]	ORR MET+ / T790M+ 55% ORR MET+ / T790M- 61%	2021
	NSCLC -2/3L 3 <sup>rd</sup> Gen EGFR TKI refract, Tagrisso combo (MET+)	Single arm Phase II/III	Global	AZ pivotal study to initiate in H2 2018	ORR MET+ 33%	2020
	<b>NEW</b> NSCLC - MET Exon14m / deletion	Single arm Phase II	China	Enrolling	China regulatory support if agreed efficacy threshold met	2020
FRUQ	3L (or above) Colorectal cancer ("CRC")	Pivotal Phase III	China	Completed, NDA submitted	✓	March 3, 2017
	3L Non-small cell lung cancer ("NSCLC")	Pivotal Phase III	China	Enrollment complete		Q4 2018 (top-line results)
	2L Gastric cancer combo with Taxol	Pivotal Phase III	China	Enrolling		Mid-2019 (interim) 2020 (top-line)
SULF	Pancreatic neuroendocrine tumors	Pivotal Phase III	China	Enrolling		H2 2019 (interim) H1 2020 (top-line)
	Non-pancreatic neuroendocrine tumors	Pivotal Phase III	China	Enrolling		H1 2019 (interim) H2 2019 (top-line)
	<b>NEW</b> 2L chemo-refractory biliary tract cancer ("BTC")	Pivotal Phase III	China	Initiating in H1 2019		2021
EPIT	1L EGFR-mutant NSCLC with brain metastasis	Pivotal Phase III	China	Initiating in H2 2018		2020

# Fruquintinib set for approval in 3<sup>rd</sup>-line CRC

Many "firsts" for China-based biotech & mainstream cancer drug



Shanghai Food and Drug Administration (SHFDA)



National Institutes for Food and Drug Control (NIFDC)



Center for Drug Evaluation (CDE)



Center for Food and Drug Inspection (CFDI)



Critical Path

# ...fruquintinib approval is just the start

Near-term readouts in NSCLC & gastric (IA [1]) & global plan...

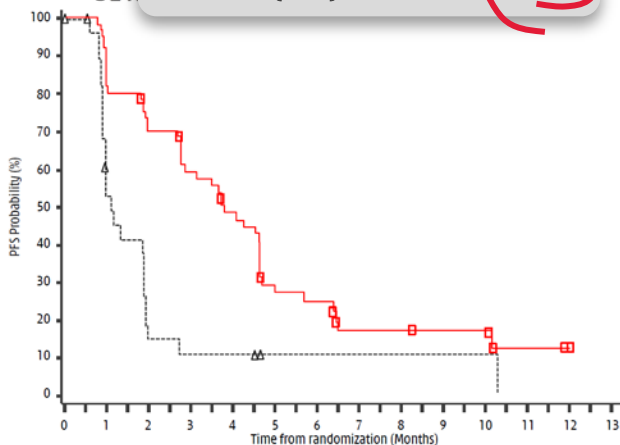


## NSCLC

- **FALUCA** China Ph.III in 3L NSCLC fully enrolled 527 patients.
- **OS maturity & top-lines expected in late 2018.**

Positive Phase II outcome (2014) in 3L NSCLC - powered for PFS (n=91):

Fruquintinib mPFS: **3.8mo.**  
Placebo (BSC) mPFS: **1.1mo.**

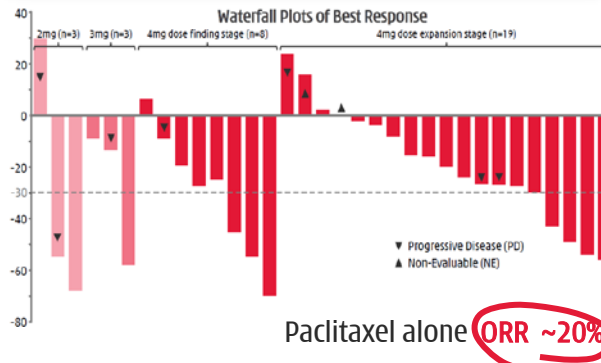


## Gastric cancer

- **FRUTIGA** China Ph.III in 2L gastric in combo with paclitaxel underway.
- **Interim analysis planned in 2019.**

Positive single-arm Phase Ib outcome (2015) in 2L gastric - ORR (n=28):

**ORR of 36%** and **DCR of 68%** in efficacy evaluable pts. Fruquintinib 4mg **≥16wk.**  
**PFS of 50%** & **OS of 50%**

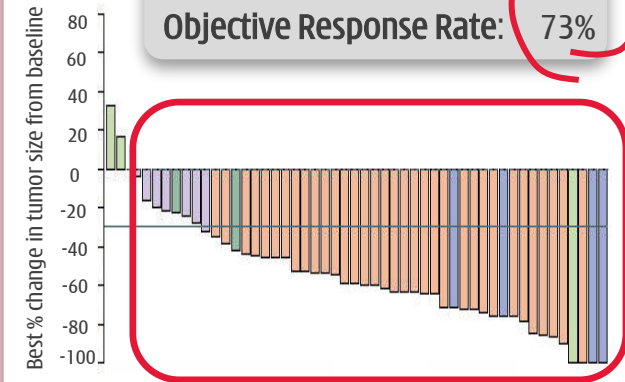


## Global expansion

- U.S. Phase I study completed YE 2018.
- **Plan for combination opportunities with immunotherapy agents.**

e.g. axitinib (VEGFR) + pembro (PD-1) in 1L ccRCC - ASCO 2018

Complete Response: **8%**  
Objective Response Rate: **73%**



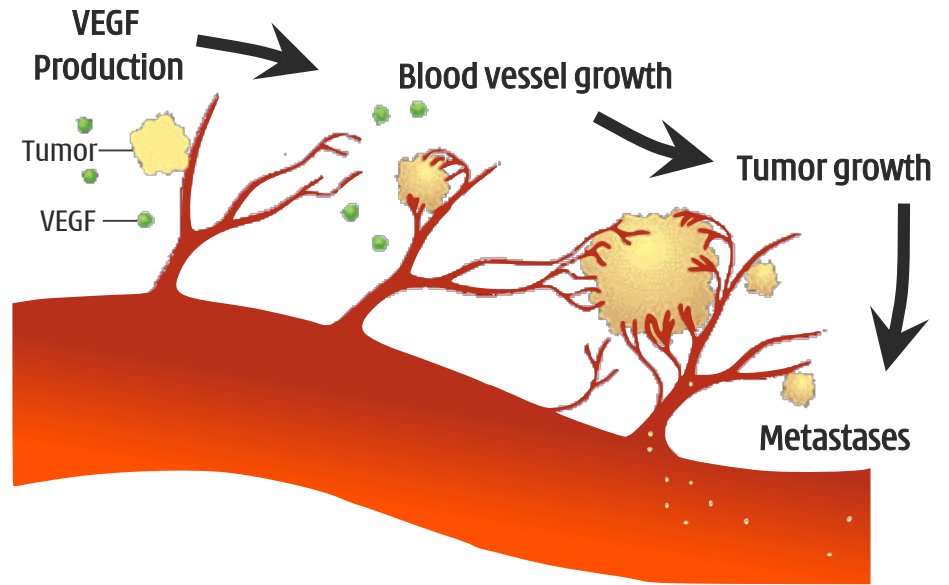
# Fruquintinib best-in-class VEGFR TKI

Cutting off blood flow<sup>[1]</sup> a **~\$18 bn** market incl. **~30 tumor settings**



Company	Drug (INN Name)	FDA Approved Indications Indication	Year	2017 Sales
Roche	Avastin® (Bevacizumab)	2L bevacizumab-pretreated mCRC	2013	\$6,796.0m
		1/2L mCRC	2004	
		1L non-sq NSCLC	2006	
		2L GBM	2009	
		1L ccRCC	2009	
		1L Cervical Ca.	2014	
		1L Ovarian Ca.	2018	
		1/2L platinum-sensitive Ovarian Ca.	2016	
		2/3L platinum-resistant Ovarian Ca.	2014	
Pfizer	Sutent® (Sunitinib)	2L GIST	2006	\$1,081.0m
		≥1L pNET	2011	
		adjuvant RCC	2017	
		1L RCC	2007	
		≥2L cytokine-ref. ccRCC	2006	
Boehringer Ingelheim	Vargatef® Ofev® (Nintedanib)	2L adeno-NSCLC (by EMA)	2014	\$1,076.0m <sup>[2]</sup>
Bayer	Nexavar® (Sorafenib)	≥1L RCC	2005	\$923.2m
		1L HCC	2007	
		Iodine-ref. DTC	2013	
Novartis	Votrient® (Pazopanib)	1/2L RCC	2009	\$808.0m
		2L STS	2012	
Lilly	Cyramza® (Ramucirumab)	2L GC	2014	\$758.3m
		2L NSCLC	2014	
		2L mCRC	2015	
Exelixis/ Ipsen	Cometriq® Cabometyx® (Cabozantinib)	≥1L MTC	2012	\$406.2m
		1L ccRCC	2017	
		≥2L ccRCC	2016	
Bayer	Stivarga® (Regorafenib)	3L mCRC	2012	\$348.7m
		2L GIST	2013	
		2L HCC	2017	
Pfizer	Inlyta® (Axitinib)	2L ccRCC	2012	\$339.0m
Merck/ Eisai	Lenvima® (Lenvatinib)	Iodine-ref. DTC	2015	\$295.9m
		2L ccRCC	2016	

Company	Drug (INN Name)	FDA Approved Indications Indication	Year	2017 Sales
Takeda	Iclusig® (Ponatinib)	CML	2012	\$237.9m
		Ph+ ALL	2012	
Hengrui	AiTan® (Apatinib)	3L GC (by CFDA)	2015	\$230.0m
Sanofi	Zaltrap® (Ziv-Aflibercept)	2L mCRC	2012	\$83.0m
Simcere	Endu® (rh-Endostatin)	≥1L NSCLC (by CFDA)	2005	\$58.1m
Sanofi	Caprelsa® (Vandetanib)	≥1L MTC	2011	NA
Aveo	Fotivda® (Tivozanib)	1/2L ccRCC (by EMA)	2017	NA
Sino Biopharm	FocusV® (Anlotinib)	3L NSCLC (by CFDA)	2018	NA



[1] Anti-angiogenesis through therapies that inhibit the vascular endothelial growth factor receptor (VEGFR) pathway. [2] Includes sales for idiopathic pulmonary fibrosis.

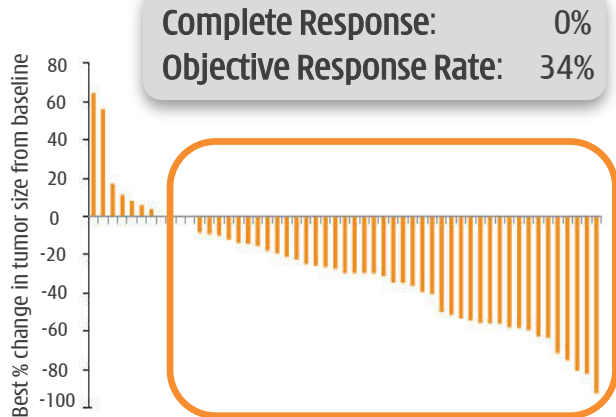
1,2 Sources: FDA approved labels; Medtrack; corporate reports; D. Ribatti, *Sales for anti-angiogenic drugs*, *Oncotarget* 2017 8(24) 38080-1.

# VEGFR combinations with immunotherapy

...delivering breakthrough efficacy...major global potentials

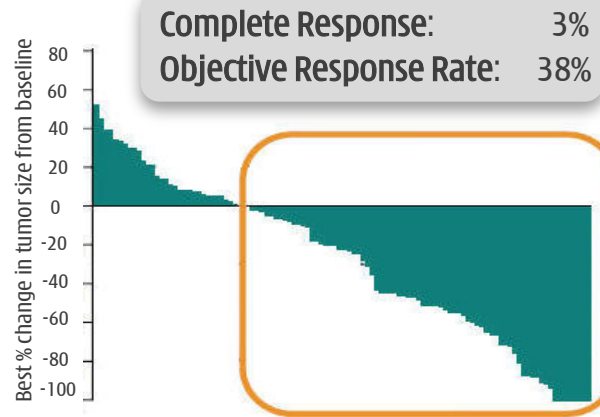


## Axitinib (VEGFR) monotherapy in 1L ccRCC



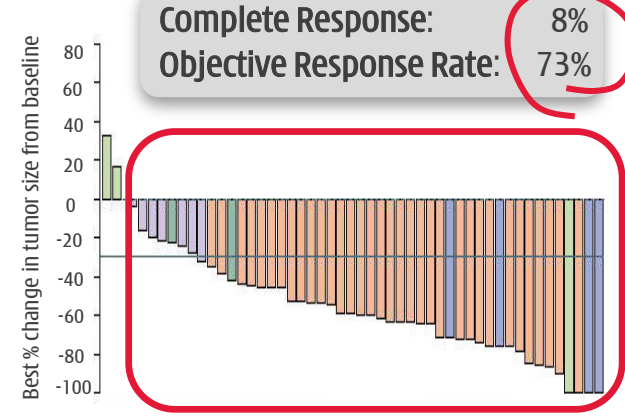
75% patients (n=56) experienced a reduction in tumor burden

## Pembrolizumab (PD-1) monotherapy in 1L ccRCC



67% patients (n=110) experienced a reduction in tumor burden

## Axitinib + Pembrolizumab combination in 1L ccRCC



96% patients (n=52) experienced a reduction in tumor burden

- Both axitinib & pembrolizumab provide strong single-agent efficacy to clear cell renal cell carcinoma patients ("ccRCC").
- Shows that both VEGFR & PD-1 inhibition are important targets.

- ...but axitinib/pembro combo provides breakthrough efficacy.
- U.S. FDA BTM<sup>[1]</sup> granted Jul 2017.**

[1] BTM = Breakthrough Therapy Designation; Source: 1. B. Rini et al, Lancet Oncol 2013 14(12) 1233-42, Axitinib with or without dose titration for first-line metastatic renal-cell carcinoma: a randomised double-blind phase 2 trial; 2. D.F. McDermott et al, ASCO 2018 #4500, Pembrolizumab monotherapy as first-line therapy in advanced clear cell renal cell carcinoma (ccRCC): Results from cohort A of KEYNOTE-427; 3. M.B. Atkins et al, Lancet Oncol 2018 19(3) 405-15, Axitinib in combination with pembrolizumab in patients with advanced renal cell cancer: a non-randomised, open-label, dose-finding, and dose-expansion phase 1b trial. Corporate press release.

# Fruquintinib & sulfatinib both unique VEGFR TKIs

...ideal VEGFR combination partners for immunotherapy

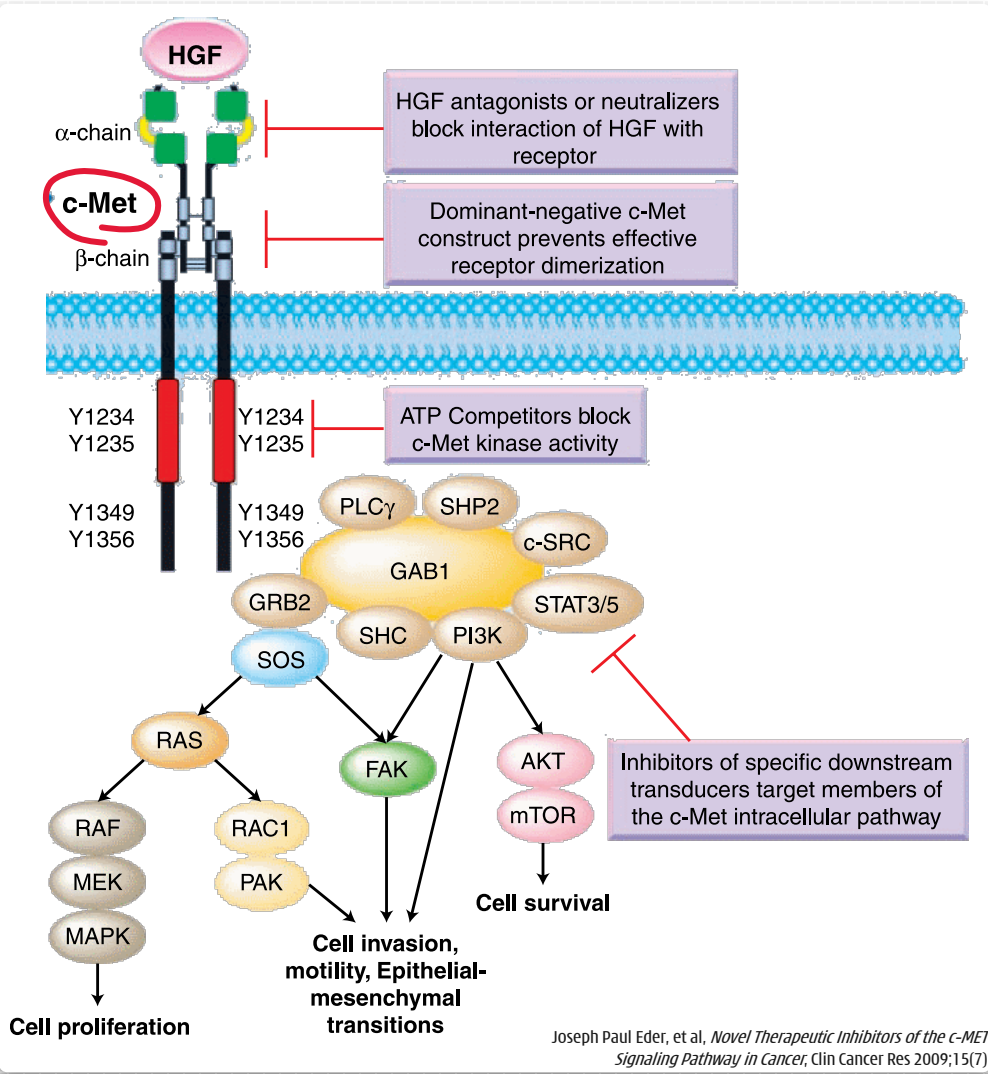


TKI	1 <sup>st</sup> Generation			2 <sup>nd</sup> Generation			Next Generation	
Selectivity	Multiple targets			Relatively selective			Highly selective	Selective angio-immuno kinase inhibitor
Inhibitors	Sunitinib	Sorafenib	Anlotinib	Tivozanib	Lenvatinib	Axitinib	Fruquintinib	Sulfatinib
Status	Launched	Launched	Launched	Launched	Launched	Launched	Approved	Ph. IIIs ongoing
VEGFR1 (nM)	2	26	27	30	22	3	33	2
VEGFR2 (nM)	9	90	0.2	6.5	4	7	25	24
VEGFR3 (nM)	19	20	0.7	15	5	1	0.5	1
Phos-KDR (nM)	10	30	0.1-1	0.16	0.8	0.2	0.6	2
Other kinases (IC <sub>50</sub> < 100nM)	PDGFR $\alpha$ PDGFR $\beta$ c-Kit Flt3 Ret CSF-1R	Raf-1 b-raf Flt3 P38 c-Kit Ret	PDGFR $\alpha$ PDGFR $\beta$ FGFR1-4 c-Kit	PDGFR $\alpha$ PDGFR $\beta$ EphB2 c-Kit Tie2	PDGFR $\alpha$ PDGFR $\beta$ FGFR1-4 Ret c-Kit	PDGFR $\alpha$ PDGFR $\beta$ c-Kit	none	CSF-1R FGFR1 FLT3 TrkB
Patent Expiration				2021/10/19 (US7253286B2)		2025/04/29 (US6534524B1)	2029 (without extension)	2030 (without extension)

- Fruquintinib is uniquely selective - unlike other TKIs with off-target toxicity.
- Sulfatinib - inhibits TAM<sup>[1]</sup> production, allowing PD-1 induced immune response.

# Savolitinib

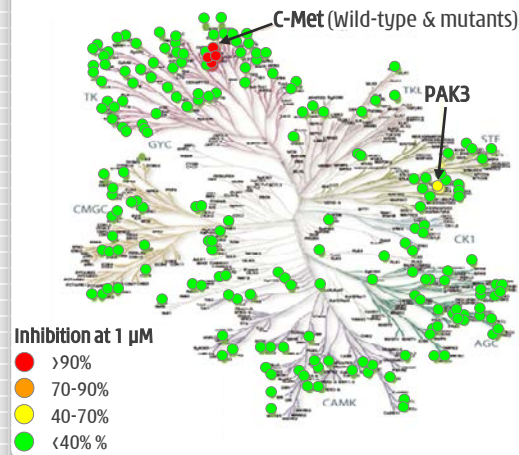
Potential first-in-class selective c-Met inhibitor...



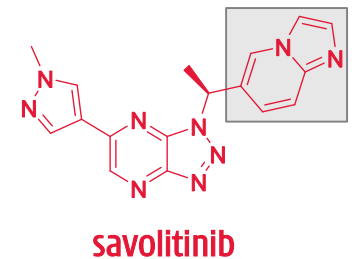
...c-Met is aberrant in many tumor settings. [3]

Indication	c-MET			New Cases (2015)	
	Amplification	Mutation	Over-Expression	Global	China
Gastric	10%	1%	41%	1,034,000	679,100
Lung	8-10% [1]	8%	67%	1,690,000	733,300
Head & Neck		11%	46%	740,000	135,000
Colorectal	10%		65%	1,477,000	376,300
Renal cell Carcinoma (Papillary)	40-70%	100% [2]		50,000	7,000
Renal cell Carcinoma (Clear cell)			79%	270,000	60,000
Esophagus	8%		92%	496,000	477,900
Prostate [4]			54-83%	1,100,000	60,300

Screening at 1 $\mu$ M against 253 Kinases



Savolitinib is **~1,000x** more selective against c-Met than next kinase (PAK3):



[1] Range includes (i) approximately 4% of c-Met+ naïve non-small cell lung cancer patients and (ii) 10 - 30% of EGFR+ non-small cell lung cancer patients, which 15 to 20% develop EGFR+ tyrosine kinase inhibitor resistance pathway as c-Met+; [2] Hereditary papillary renal cell carcinoma only; [3] Company estimates considering Frost & Sullivan data, National Central Cancer Registry of China and publicly available epidemiology data. [4] By IHC, c-Met overexpression in 54% of lymph node disease and 83% of bone metastases. Varkaris et al, Expert Opin Investig Drugs. 2011 Dec; 20(12): 1677-1684.

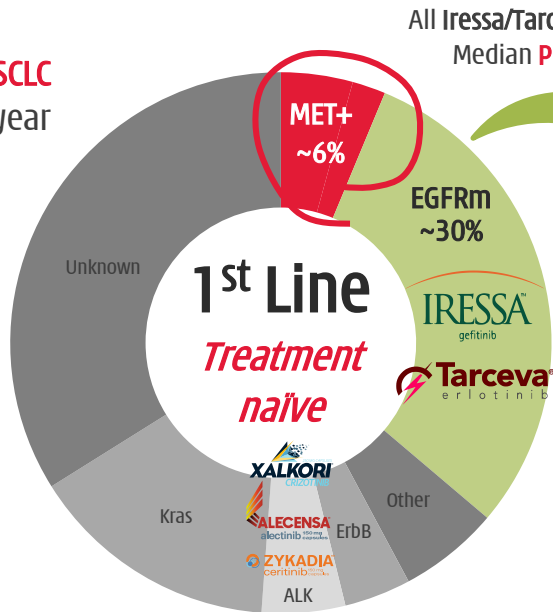
# Savolitinib

Biggest opportunity is MET+ non-small cell lung cancer ("NSCLC")

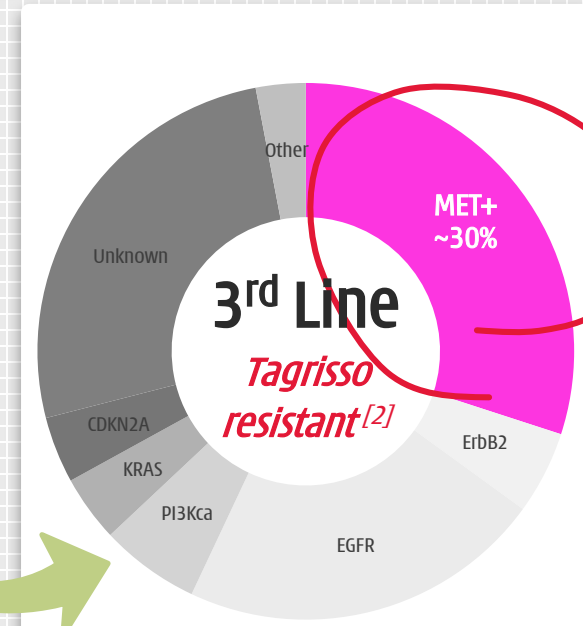
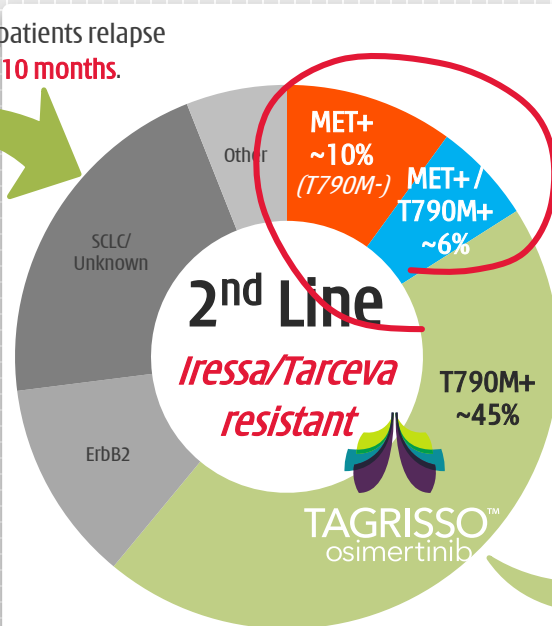


## Primary NSCLC

1.7 million NSCLC patients per year



## Resistance-driven EGFRm+ NSCLC



	Target	Launch	2017 (\$m)	Est. <sup>[1]</sup> Pts Treated/yr.
Iressa	EGFRm	2003	528	~20,000
Tarceva	EGFRm	2004	860	~50,000
Tagrisso	EGFRm / T790M	2018		
Xalkori	ALK / ROS1 / MET	2011	594	
Zykadia	ALK	2015	Not disc.	
Alecensa	ALK	2015	369	
<b>Total Sales</b>			<b>&gt; 2.3b</b>	

Launch	2016 (\$m)	2017 (\$m)	H1 2018 (\$m)	Est. <sup>[3]</sup> Pts Treated/yr.
Dec-15	423	955	760	~5-10,000
	423	955	760	

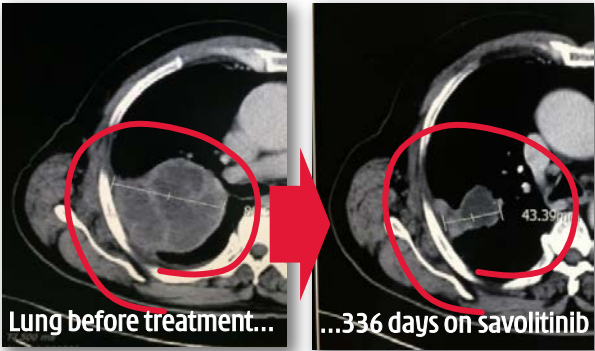
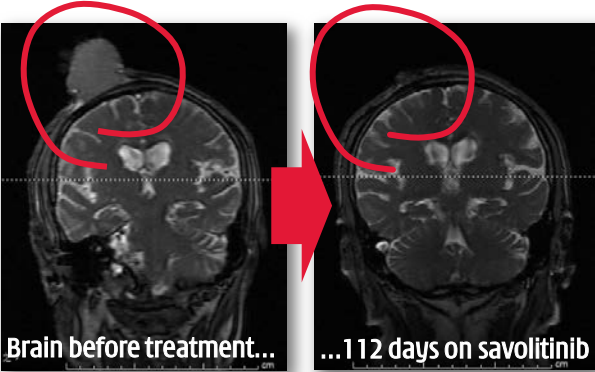
**Est. global peak sales ~\$3-4 bn<sup>[4]</sup>.**

16 [1] General estimate based on mPFS ~9 mo. average cost/cycle ~\$2,500-3,000; [2] Primary drivers, based on aggregate rocletinib/Tagrisso data published at 2016/2017 ASCO; [3] AstraZeneca 2016 /17 results; [4] Company estimates.



# Savo standout efficacy in all MET+ NSCLC subsets...

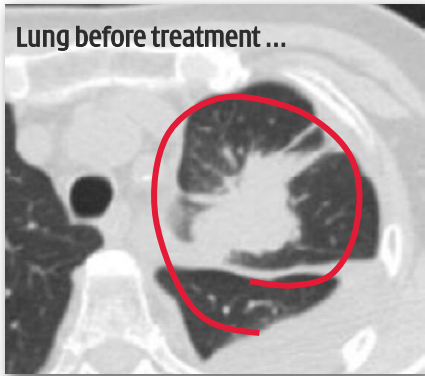
## 1L NSCLC [1]



## 2L post Iressa® / Tarceva®



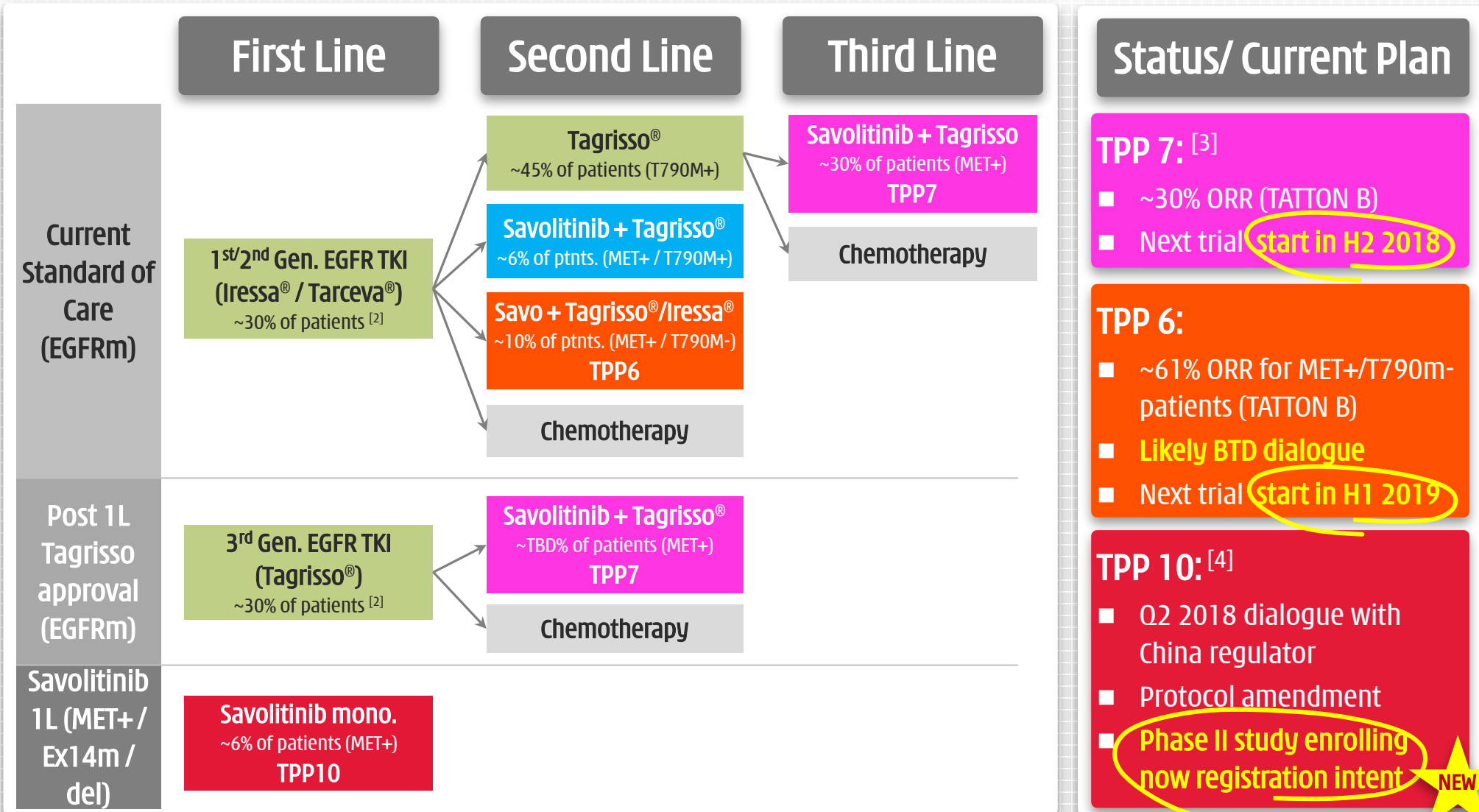
## 2L/3L post Tagrisso®



[1] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients.

# Savo in NSCLC

Multiple potential registration studies<sup>[1]</sup> underway or in planning



[1] Subject to upcoming/future regulatory dialogue; [2] General estimate based on EGFRm prevalence in approx. 10-15% of Caucasian NSCLC patients & 50-60% of Asian NSCLC patients; [3] TPP = Target Patient Population;

[4] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients.

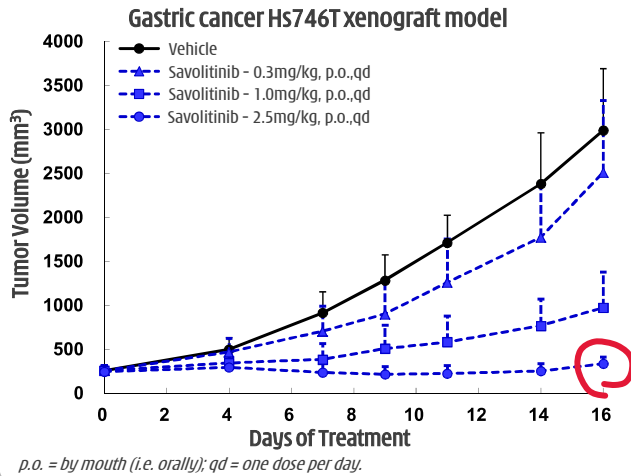


# Savo potential not only in NSCLC...

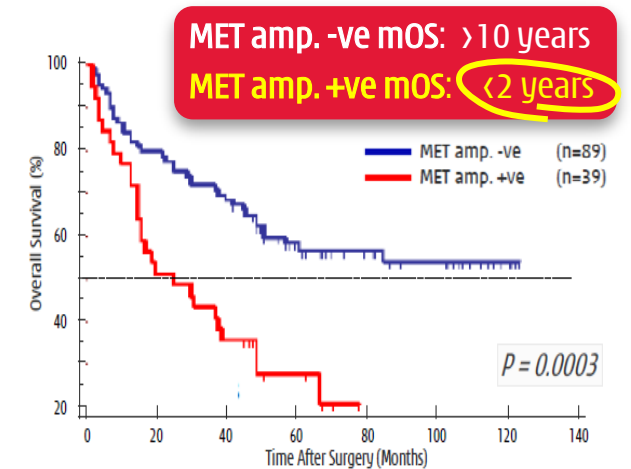
...highly promising efficacy in MET+ gastric cancer (...& kidney)



## Strong preclinical efficacy.



## MET+ gastric - very poor survival.<sup>[1]</sup>



## 3. VIKTORY trial - 34-year old male; surgery ruled-out; failed 4-cycles XELOX.



# Sulfatinib - global development

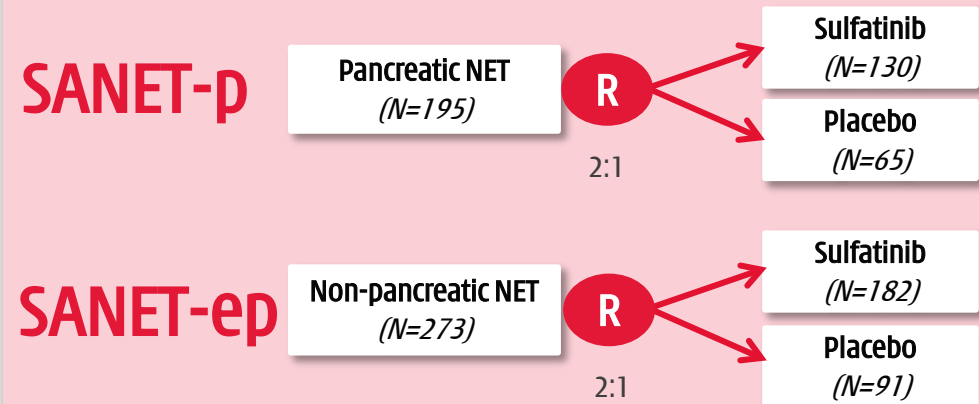
First un-partnered asset through China PoC & started US study



## Pancreatic NET ("P-NET") & Non-Pancreatic NET ("EP-NET")

- SANET-p & SANET-ep active in **25 China sites**;
- Target to conduct **Interim Analysis in 2019** on SANET-ep in H1 2019 & SANET-p in H2 2019;
- Enrolment expected for both Phase III studies to **complete late 2019 / early 2020**;
- Potential **launch in China in late 2020 / 2021** - first un-partnered oncology asset for Chi-Med.

### China Phase III study design:



## Biliary Tract Cancer ("BTC")

- **Clear unmet medical need** - a few agents being tested in 2L BTC but standard of care not yet established;
- Phase II PoC initiated in early 2017;
- **Planning for Phase III pivotal study in BTC in China is underway aiming to initiate H1 2019.**

## U.S. Development Expanding

- Phase I dose escalation study in the U.S. completed (N=29), 5 dose cohorts (50-400mg QD), established **300mg. QD as RP2D** (same as China);
- U.S. Phase Ib/II study in **P-NET & BTC initiated July 2018.**
- Chi-Med C&R Team now in place in U.S. to manage.

# Epitinib

## Progress on regulatory dialogue & design of Phase III protocol



### 1. Epitinib a first-generation EGFR TKI w/ a highly unique blood-brain barrier penetration profile. [1]

#### ■ Clear efficacy in EGFR TKI naïve patients

- ✓ 68% ORR in lung & 70% in measurable brain lesions (excluding c-MET positive patients). [2]

#### ■ Safe & well tolerated

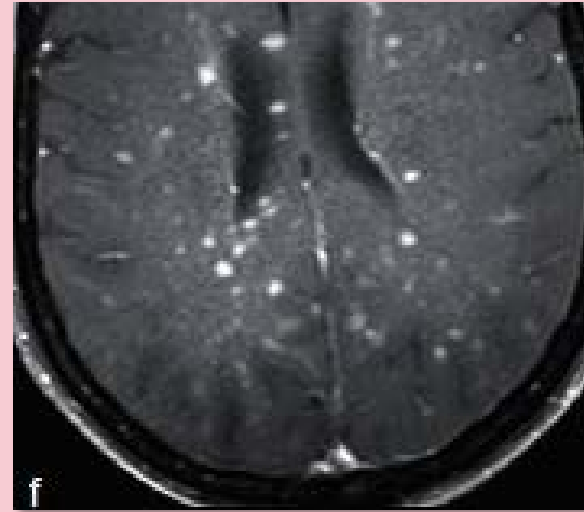
- ✓ Expanded Phase Ib in 2018 to confirm 120mg QD as the recommended Phase III dose.

### 2. Preparing to progress epitinib into Phase III in patients with EGFRm+ NSCLC w/ brain metastasis. [3]

#### ■ Design of Phase III protocol highly complex

- ✓ Multiple China CDE & PI interactions;
- ✓ Classification of CNS lesions & leptos;
- ✓ PFS endpoint, intracranial &/or extracranial PD;
- ✓ Control - changing EGFR TKI landscape.

#### ■ Almost ready to proceed - planning to initiate Phase III in late 2018.



### Stars-in-the-sky metastases

- Often asymptomatic;
- Challenging to evaluate/establish PD (Progressive Disease);
- Can be slower to PD.



### Measurable brain lesion (>10mm)

- Often symptomatic;
- RECIST1.1 - more reliable tumor evaluation;
- Can be faster to PD.

# HMPL-523 (Syk) in hematological cancer

Australia & China - large Phase Ib expansion now moving faster

■ Extensive **Ph.I dose escalation study now complete** in Australia & China (total n=60);

■ Target to present **Ph.I dose escalation data** (Australia & China, n=60) including **preliminary efficacy data at 2018 ASH** [1] (San Diego, December 2018);

■ RP2D [2] determined & **large Ph. Ib dose expansion study, total n=192**, underway in 13 active sites in Australia & China;

■ **US IND application cleared by FDA** & planning underway for a Phase II PoC [3] study

## Australia & China Phase I/Ib studies

### Stage I: dose escalation

- Australia: Relapsed/refractory hematologic malignancy
- China: Relapsed/refractory mature B lymphoma

"3 + 3" each dose cohort

N = 33

N = 27

**Complete** ✓

Studied HMPL-523  
100-1,000mg QD &  
200-400mg BID in  
13 dose cohorts

until disease progression, death, intolerable toxicity, etc.

### Stage II: dose expansion

Relapsed or refractory, measurable disease - multiple arms:

- Chronic lymphocytic leukemia
- Small lymphocytic lymphoma
- Mantle cell lymphoma
- Follicular lymphoma
- Diffuse large B-cell lymphoma

N = 40

N = 152

**...Now enrolling**

Australia  
800mg QD

China  
600mg QD

until disease progression, death, intolerable toxicity, etc.

# Pipeline Updates

*Latest updates on all clinical programs*

*Expected news flow*

# 7 registration studies underway/completed

## ....with 4 more set to start by mid 2019



Program	Target	Partner	Indication	Latest Status	Line	Target patient	Combo therapy	Site	Preclin.	Ph.I	Proof-of-concept	Registration		
Savolitinib (AZD6094)	c-Met	AstraZeneca	1. Papillary renal cell carcinoma	Ph.III enrolling	1 <sup>st</sup> /2 <sup>nd</sup>	c-Met-driven		Global				➔ 1		
			2. Papillary renal cell carcinoma	NCI Ph.II - savo vs. sunitinib vs. cabozan. vs. crizot.	All	All		US						
			3. Papillary renal cell carcinoma	Ph.II enrolling	-	All	durvalumab (PD-L1)	UK/Sp						
			4. Clear cell renal cell carcinoma	Ph.II enrolling	2 <sup>nd</sup>	VEGF TKI refractory		UK/Sp						
			5. Clear cell renal cell carcinoma	Ph.II enrolling	2 <sup>nd</sup>	VEGF TKI refractory	durvalumab (PD-L1)	UK/Sp						
			6. Non-small cell lung cancer	Ph.II enrolling; target next trial start H1 2019	2 <sup>nd</sup>	EGFR TKI refractory	Tagrisso® (T790M)	Global						➔ 1
			7. Non-small cell lung cancer	Ph.II enrolling; target next trial start H2 2018	2 <sup>nd</sup> /3 <sup>rd</sup>	EGFR/T790M TKI	Tagrisso® (T790M)	Global						➔ 2
			8. Non-small cell lung cancer	Ph.II enrollment complete; pivotal under discussion	2 <sup>nd</sup>	EGFR TKI refractory	Iressa® (EGFR)	China						
			9. Non-small cell lung cancer	Ph.II enrollment complete	1 <sup>st</sup>	c-Met-driven		China						
			10. Lung cancer	Ph.II enrolling; NMPA agrees with registration intent	1 <sup>st</sup> *	Exon 14m/del		China						➔ 2
			11. Gastric cancer	Ph.II enrolling	3 <sup>rd</sup> /All	c-Met+		SK/PRC						
			12. Gastric cancer	Ph.II enrolling	2 <sup>nd</sup>	c-Met+	docetaxel (chemo)	SK						
			13. Gastric cancer	Ph.II enrolling	2 <sup>nd</sup>	c-Met O/E	docetaxel (chemo)	SK						
			14. Prostate cancer	CCTG Ph.II enrolling - umbrella trial	1 <sup>st</sup> /2 <sup>nd</sup>	c-Met-driven		Can						
Fruquintinib	VEGFR 1/2/3	Lilly (in China only)	15. Colorectal cancer	Ph.III met all endpoints; NDA submitted Jun 2017	3 <sup>rd</sup>	All ✓		China				➔ 3		
			16. Non-small cell lung cancer	Ph.III fully enrolled; expect top-line results late 2018	3 <sup>rd</sup>	All		China			n/a		➔ 4	
			17. Non-small cell lung cancer	Ph.II enrollment complete	1 <sup>st</sup>	All	Iressa® (EGFR)	China						
			18. Solid tumors	Ph.I enrolling	-	All comers		US						
			19. Gastric cancer	Ph.III enrolling	2 <sup>nd</sup>	All	paclitaxel (chemo)	China						➔ 5
Sulfatinib	VEGFR/CSF1R/FGFR1		20. Pancreatic NET (P-NET)	Ph.III enrolling	All	All		China				➔ 6		
			21. Non-pancreatic NET	Ph.III enrolling	All	All		China					➔ 7	
			22. P-NET & biliary tract cancer	Ph.Ib/II enrolling	-	All comers		US						
			23. Medullary thyroid ca.	Ph.II enrollment complete	2 <sup>nd</sup>	Radiotherapy ref.		China						
			24. Differentiated thyroid ca.	Ph.II enrollment complete	2 <sup>nd</sup>	Radiotherapy ref.		China						
25. Biliary tract cancer	Ph.II enrolling; target Ph.III initiation H1 2019	2 <sup>nd</sup>	Chemo ref.		China						➔ 3			
Epitinib	EGFRm+		26. Non-small cell lung cancer	Preparing for Ph.III; target initiation 2018	1 <sup>st</sup>	EGFRm+ brain mets		China				➔ 4		
			27. Glioblastoma	Ph.Ib/II enrolling	-	EGFR+		China						



Registration trial underway



New registration trial in planning

Notes: Proof-of-concept = Phase Ib/II study (the dashed lines delineate the start and end of small Phase Ib); combo = in combination with; brain mets = brain metastasis; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; EGFR = epidermal growth factor receptor; NET = neuroendocrine tumors; ref = refractory, which means resistant to prior treatment; T790M = EGFR resistance mutation; EGFRm+ = EGFR activating mutations; EGFR+ = EGFR gene amplification; EGFR WT = EGFR wild-type; 5ASA = 5-aminosalicylic acids; chemo = chemotherapy; c-Met+ = c-Met gene amplification; c-Met O/E = c-Met over-expression; FGFR = Fibroblast Growth Factor Receptor; CSF1R = Colony Stimulating Factor-Receptor 1; NCI = U.S. National Cancer Institute; CCTG = Canadian Cancer Trial Group; Aus = Australia; Can = Canada; SK = South Korea; PRC = People's Republic of China; Sp = Spain; UK = United Kingdom; US = United States; Global = > 2 countries.

24 \* The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients.



# Next wave of innovation now in proof-of-concept

Program	Target	Partner	Indication	Latest Status	Line	Target patient	Combo therapy	Site	Preclin.	Ph.I	Proof-of-concept	Registration
Theliatinib	EGFR WT		28. Solid tumors	Ph.I completed	-	All comers		China				
			29. Esophageal cancer	Ph.Ib expansion enrolling	1 <sup>st</sup>	EGFR WT		China				
HMPL-523	Syk		30. Immunology	Ph.I completed; preparing for US Ph.II	-	TBD		Aus				
			31. Immunology	Ph.I dose escalation	-	Healthy volunteers		China				
			32. Hematological cancers	Ph.I enrolling	2 <sup>nd</sup> /3 <sup>rd</sup>	All comers		Aus				
			33. Lymphoma	Ph.I enrolling	-	All comers		China				
HMPL-689	PI3Kδ		34. Healthy volunteers	Ph.I complete; preparing for US Ph.II	-	Healthy volunteers		Aus				
			35. Lymphoma	Ph.I enrolling	2 <sup>nd</sup> /3 <sup>rd</sup>	All comers		China				
HMPL-453	FGFR 1/2/3		36. Solid tumors	Ph.I	-	All comers		Aus				
			37. Solid tumors	Ph.I enrolling	-	All comers		China				
HM004-6599	NF-κB	Nestlé Health Science	Ulcerative colitis	Ph.I	2 <sup>nd</sup>	5ASA refractory		Aus/China				
NSP DC2	TBD	Nestlé Health Science	Immunology	IND end of 2019				China				
Multiple	TBD		Oncology	Four small molecule/antibody programs in preclin.				TBD				

**>4,000 subjects treated in all studies (as of June 30, 2018);  
and >400 dosed in H1 2018.**

# Major targets/news flow in H2 2018 & H1 2019

**Savolitinib**

- 1. Initiate **global study** of savolitinib/ Tagrisso® combo in 2L NSCLC - **regulatory & potential BTD** [1] **dialogue** [2];
- 2. Initiate **global study** of savolitinib/ Tagrisso® combo in 2L/3L NSCLC post Tagrisso® failure; AZ presents **data on c-Met resistance**; **regulatory dialogue**;
- 3. Molecular epidemiology study (n>200) in PRCC [3] - **possibly BTD enabling**.

H1 2019

H2 2018

H2 2018

**Fruquintinib**

- 4. China **NDA approval & launch** in 3L CRC;
- 5. Report **top-line data for Phase III** FALUCA study in 3L NSCLC.

H2 2018

H2 2018

**Epitinib**

- 6. Initiate **China Phase III** study in 1L EGFRm NSCLC w/ brain mets.

H2 2018

**Sulfatinib**

- 7. Initiate **China Phase III** study in chemo-refractory BTC.

H1 2019

**HMPL-523**  
*(Syk)*

- 8. Potential presentation of prelim. **safety & efficacy data** from Phase I dose escalation studies in hematological cancer.

H2 2018

**HMPL-689**  
*(PI3Kδ)*

- 9. Present Phase I dose escalation data in Australian healthy volunteers.

H1 2019

High impact

Impact

A close-up photograph of a male doctor with dark hair and glasses, wearing a white surgical mask and a white lab coat over a light-colored button-down shirt. A red stethoscope is visible around his neck. He is looking slightly to the right of the camera. The background is blurred, showing another person's head in the foreground on the right.

# China Commercial Updates

*H1 2018 performance*

# Chi-Med's Commercial Platform in China

Built from ground up - track record of success - source of cash



## 2 National household name brands



## Focus on largest disease categories

Most common disease diagnosed/treated in rural hospitals [1]:

Cold/Flu:	86%
Cardiovascular:	78%
Diabetes:	46%
GI:	45%

## Major commercial & production scale

~2,400 RX & ~1,000 OTC sales people in about 300 [2] cities & towns in China.

Drugs in ~22,900 hospitals detailing ~106,000 doctors.  
Sold ~4.6 billion doses of medicine in 2017.

## Leadership market shares

Market leader in the sub-categories/markets in which we compete [3]:

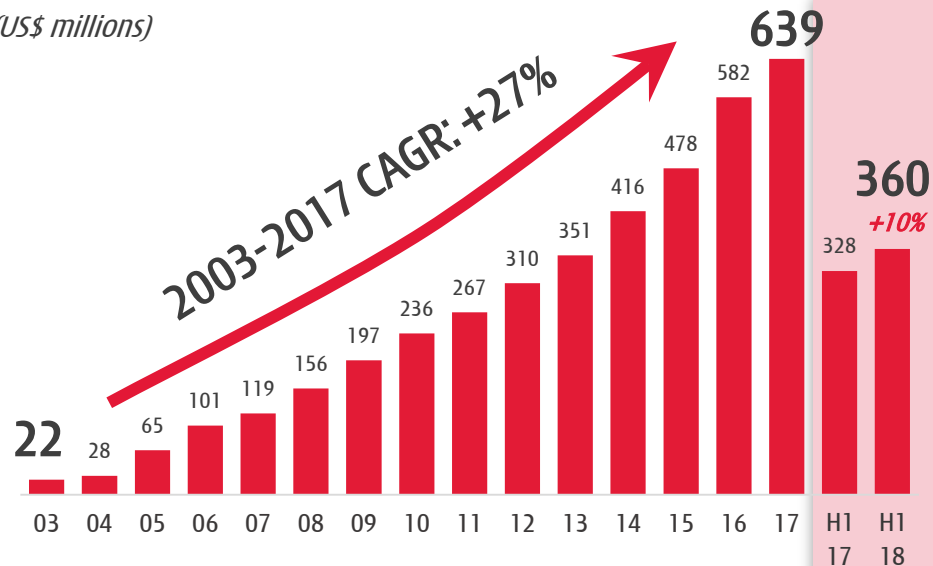
SXBX pill:[4][5] Rx Cardiovascular TCM	~15%
Banlangen:[6] OTC Anti-viral /flu TCM	~53%
FFDS tablet:[7] OTC Angina TCM	~38%

## JVs with 3 major China Pharmas



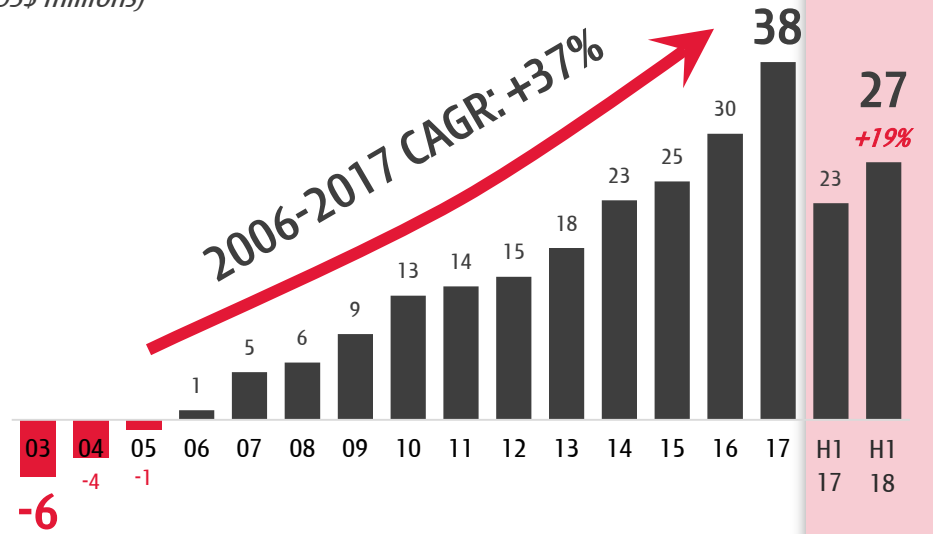
## Commercial Platform - Sales (Non-GAAP) [8][9]

(US\$ millions)



## Commercial Platform - Net Income/(Loss) attrib. to Chi-Med [8][9]

(US\$ millions)



[1] Frost & Sullivan; [2] 300 cities & towns covered by Prescription Drug Business and 600 cities & towns including OTC business; [3] Frost & Sullivan 2017 market share data; [4] China coronary heart disease oral Chinese patented drugs market share; [5] She Xiang Bao Xin Pill ("SXBX pill"); [6] Banlangen Granules ("Banlangen") - OTC Antiviral; [7] Fu Fang Dan Shen tablets ("FFDS"); [8] 2003-2006 incl. disco. operation; [9] 2011-2017 and H1 2017 sales (Non-GAAP) excluding GuanBao which was divested in Sept 2017; 2016-2017 and H1 2017: Net income/(loss) attributable to Chi-Med excluding SHPL's one-off land compensation and government subsidies.

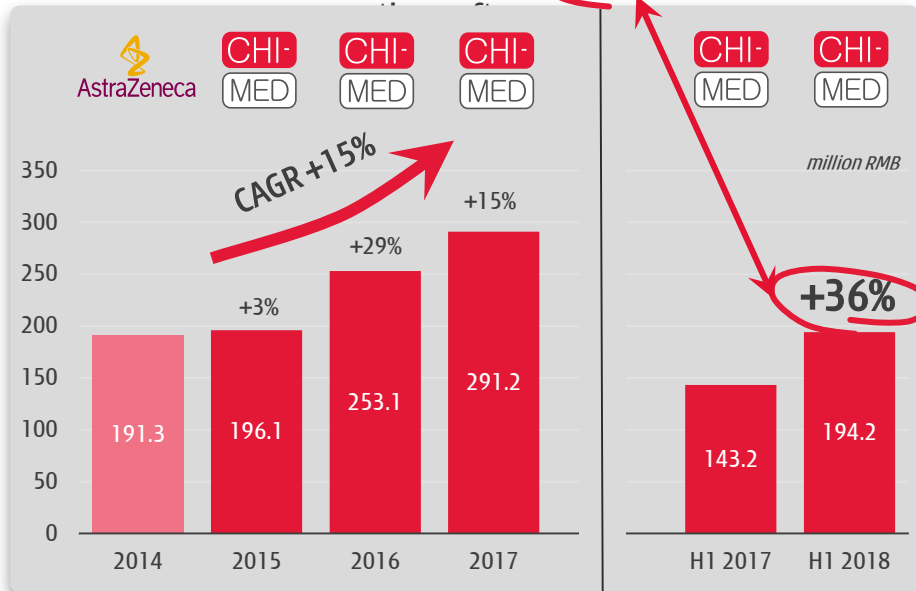
# ...highly adaptable commercial platform

3<sup>rd</sup> party products - sales of Seroquel® & Concor® up significantly



Seroquel®, or quetiapine, is a second generation antipsychotic approved for the treatment of schizophrenia, bipolar disorder and as adjunct treatment of major depressive disorder.

- Chi-Med holds **exclusive all China commercial rights** - full service commercial role (fee-for-service<sup>[1][2]</sup>).
- Luye acquisition has no effect. **Chi-Med retains rights through 2025 if we hit sales targets. 2018 target RMB354m or +22% & +15% p.a.**



**Service fees: \$4.9m \$9.3m \$11.4m**  
(Paid to Chi-Med)

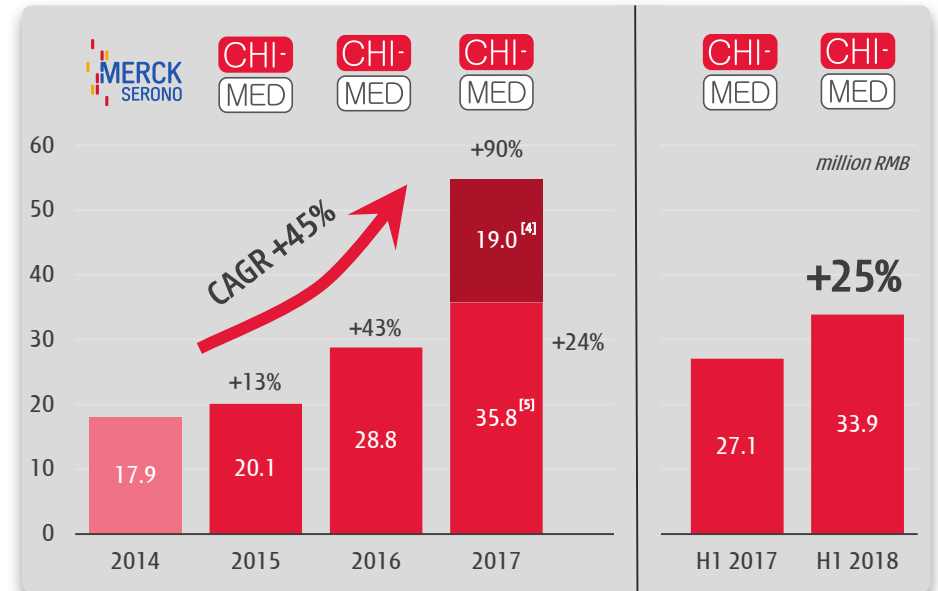
**\$5.5m \$9.6m**  
US\$ million

[1] In Oct 2017, as a result of the new NMPA Two-Invoice System policy, the Seroquel® operating model changed to a "fee-for-service" model vs. the prior model in which Chi-Med consolidated the sales of Seroquel® -- the change has no material impact on net income earned;  
[2] 2014 full year and Q1 2015 were managed by AstraZeneca. Chi-Med took over commercial function for Seroquel® across all-China in April 2015.



Concor®, or bisoprolol hemifumarate, is a beta-blocker approved for the treatment of hypertension.

- Chi-Med runs **six core territories covering 360m people** - full service commercial role (fee-for-service).
- Took over from MS Jan-2015<sup>[3]</sup>.
- Leverages SHPL's existing **>2,200 cardiovascular medical reps.**



**Service fees: \$0.9m \$1.4m \$1.8m**  
(Paid to Chi-Med)

**\$1.1m \$2.2m**  
US\$ million

[3] 2014 full year was managed by Merck Serono. Chi-Med took over commercial function for Concor® in 3 original territories on fee-for-service basis in Jan 2015; [4] Sales into 3 new territories (Tianjin, Anhui and Jiangsu) were added from 2017: RMB19.0 million; [5] 3 original territories (Shandong, Henan and Shanghai) contributed RMB35.8 million in 2017 (+24.3%).

The background is a collage of images related to pharmaceutical research and development. It includes a close-up of a person in a white lab coat using a pipette to transfer liquid into a multi-well plate. Another person is seen from behind, drawing chemical structures on a whiteboard. At the bottom, there is an image of a modern laboratory with two scientists working at a bench, and a large, multi-story white building with a red stripe and Chinese characters, likely a pharmaceutical facility.

# Innovation Platform

*Near term: Driving for first product launches*

*Mid-longer term: Building the pipeline for future growth*

# Exceptional scale for pre-approval biotech

Over 16 years with about **\$590 million** invested to-date



**~390 SCIENTISTS & STAFF** [1]

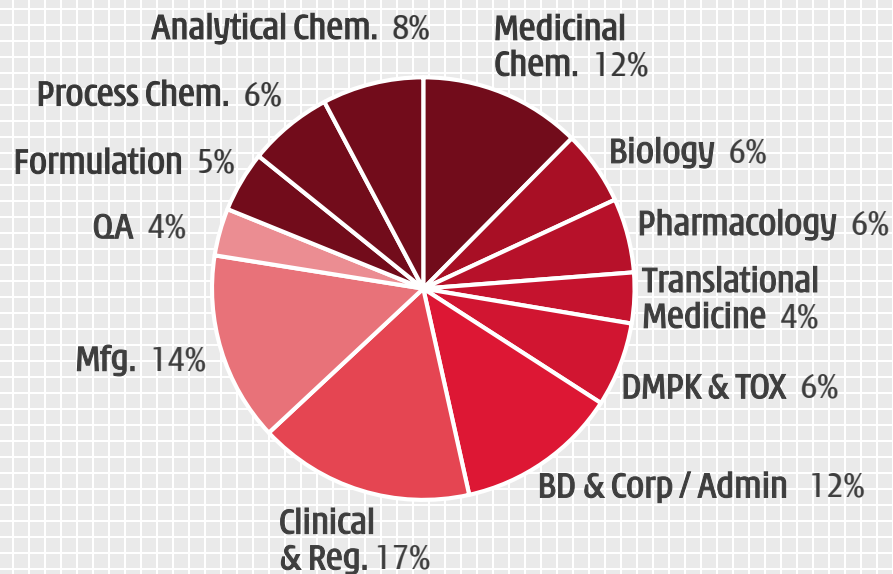
- ✓ **217 with advanced technical degrees**
- ✓ **25 M.D.s**
- ✓ **53 doctorate degrees**

✓ **Large-scale fully integrated in-house platform**  
chemistry, biology, pharmacology, DMPK, toxicology, CMC, clinical & regulatory, and translational organizations working together seamlessly and continuously.

✓ **China clinical speed**  
major unmet medical needs (4.3 million new cancer patients / year<sup>[2]</sup>), rapid development and regulatory support. Allows for study of multiple indications and proof-of-concept in China.

✓ **Competitive costs**  
overall clinical costs, particularly pre-PoC, a fraction of US or Europe.

✓ **Constancy of purpose**  
Over 16 years with stable financial support.



[1] Headcount as of June 30, 2018; Chem. = Chemistry; DMPK = Drug, Metabolism, & Pharmacokinetics; Tox. = Drug Safety Evaluation; QA: Quality Assurance; Mfg. = Manufacturing; Reg. = Regulatory; BD = Business Development; [2] CA Cancer J Clin 2016;66:115-132. 2016 American Cancer Society.

# Chemistry is our edge

## Seriously selective small molecules

### 1. Fragment-based design of Novel Chemical Entities.

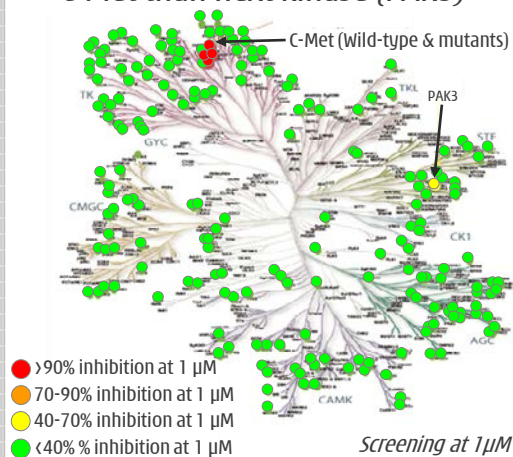
- Internally designed (all 8) clinical drug candidates.
- Use of co-crystal structures.
- Focus on small molecule interactions with tyrosine kinases - proteins/enzymes involved in cell signaling.

### 2. Total focus/discipline in designing and progressing drug candidates with superior kinase selectivity.

- Optimize binding to on-target protein, minimize off-target protein binding.
- No off-target kinase inhibition gives compound the chance to be more potent, attaining better target coverage with less toxicity.
- Combinability - clean compounds allow for combinations with other tyrosine kinase inhibitors ("TKIs"), immunotherapy & chemotherapy agents.

### Savolitinib [1]

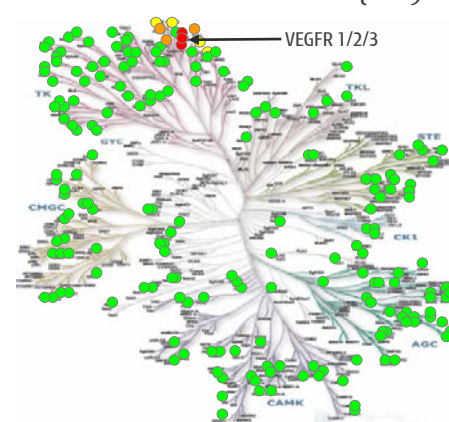
~1,000 times more selective to *c-Met* than next kinase (PAK3)



Screening at 1 μM against 253 Kinases

### Fruquintinib [2][3]

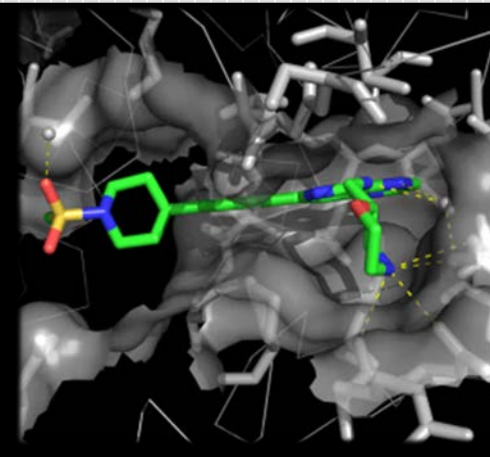
~250 times more selective to *VEGFR3* than next kinase (*Ret*)



### Use of co-crystal structures

Focus on small molecule interactions with kinases

- ✓ Optimize binding to on-target protein, for potency.
- ✓ Minimize binding to off-target proteins for selectivity.





# Superior selectivity = Better tolerability

Long-term use = prolonged/total target coverage = better efficacy

## 3. Monotherapies - 1<sup>st</sup> generation TKIs not optimal for long-term use

- Multi-kinase TKIs - major dose modifications **due to off-target toxicities.**
- Chi-Med's **more selective TKIs designed for less dose modifications & discount.**

EXAMPLES OF MONOTHERAPY APPROVED SMALL MOLECULE TKIS - targets (approval yr.)	2017 Sales	Recent Monotherapy Cancer Trial [2]	mPFS (months)	Dose Reductions	Discont. due to AEs	Total Discontinuations
<b>Sutent® (sunitinib)</b> - VEGFR1,2,3, PDGFRβ, FLT3, CSF-1R, c-Kit, Ret (2006)	\$1.08b	1L ccRCC (CABOSUN) 1L ccRCC (COMPARZ)	5.6 9.5	49% 51%	22% 18%	38% 33%
<b>Nexavar® (sorafenib)</b> - RAF, VEGFR2, PDGFRβ, Flt3, c-Kit, FGFR1 (2005)	\$0.94b	2L RCC (AXIS)	5.7	54%	13%	23%
<b>Votrient® (pazopanib)</b> - VEGFR1,2,3, c-KIT, ITK, LCK, PDGFRα,β, FGFR1,3, c-Fms (2009)	\$0.81b	1L ccRCC (COMPARZ)	8.4	44%	23%	36%
<b>Inlyta® (axitinib)</b> - VEGFR1,2,3, PDGFRα, c-Kit (2012)	\$0.34b	2L RCC (AXIS)	8.3	34%	8%	17%
<b>Cabometyx® (cabozantinib)</b> - AXL, c-Kit, FLT3, MET, RET, TIE-2, TrkB, VEGFR1,2,3 (2016)	\$0.35b	1L ccRCC (CABOSUN)	8.2	58%	21%	27%
<b>Lenvima® (lenvatinib)</b> - VEGFR1,2,3, Ret, PDGFR, c-Kit, FGFR1,2,3,4 (2015)	\$0.27b	2L ccRCC (Ph 2 reg.)	7.4	62%	25%	31%
<b>Stivarga® (regorafenib)</b> - VEGFR1,2,3, Raf, Ret, PDGFR, c-Kit (2012)	\$0.36b	≥3L CRC (CORRECT) ≥3L CRC (CONCUR China)	1.9 2.0	20% 23%	8% 14%	21%
<b>savolitinib</b> - c-Met (Ph II)		pRCC (JCO 2017)	6.2 (c-MET+)	13%	8%	14%
<b>fruquintinib</b> - VEGFR1,2,3 (FRESCO)		≥3L CRC	3.7	24%	15%	19%
<b>fruquintinib</b> - VEGFR1,2,3 (Ph II)		3L NSCLC	3.8	13%	8%	11%
<b>sulfatinib</b> - VEGFR 1,2,3, FGFR1, CSF-1R (Ph II)		PNET, EP-NET	19.4, 13.4	25%	9%	19%
<b>epitinib</b> - EGFR (Ph I/II)		NSCLC w/brain mets		6%	N/D	N/D

## 4. Combination therapies proving to be a hard challenge

- Avg. 64% with grade 3-4 tox. vs. 37% in mono. trials.<sup>[1]</sup>
- ≤10 TKI+TKI or TKI+IO oncology combos FDA approved (as of YE 2017).<sup>[3]</sup>
  - ✗ Drug-drug interactions.
  - ✗ Overlapping AEs.
- Keys to sustained combo use (i.e. minimize discount.):
  - ✓ Constituents **must be highly tolerable.**
  - ✓ **Clear known AE profiles & careful management.**

[1] Roda D et al. Clinical Cancer Research 2016 May 1;22(9):2127-32; [2] Sources: CABOSUN = Choueiri et al. J Clin Oncol. 2017 Feb 20;35(6):591-597; COMPARZ = Motzer et al. N Engl J Med. 2013 Aug 22;369(8):722-31; AXIS = Motzer et al. Lancet Oncol. 2013 May;14(6):552-62; lenvatinib Ph 2 = Motzer et al. Lancet Oncol. 2015 Nov;16(15):1473-82; CORRECT = Grothey et al. Lancet. 2013 Jan 26;381(9863):303-12; CONCUR China = Xu et al. "Efficacy and safety of regorafenib monotherapy in Chinese patients with previously treated metastatic colorectal cancer", CSCO 2014; savolitinib PRCC = Choueiri et al. J Clin Oncol. 2017 Sep 10;35(26):2993-3001; FRESCO = Li et al. J Clin Oncol. 2017 May 35(15\_suppl):3508-3508; fruquintinib NSCLC = Liu, ID4571, WCLC 2017; sulfatinib NET = Xu et al. #1697, ENETS 2017; epitinib NSCLC = Chi-Med data; [3] Approved TKI combos: HER2 inhibitor + HER2 inhibitor; BRAF inhibitor + MEK inhibitor; VEGFR inhibitor + MTOR inhibitor; PI3K6 inhibitor + CD20 inhibitor. Also approved - IO combo of PD-1 inhibitor + CTLA4 inhibitor; N/D = not disclosed; Total Discontinuations = Discontinuations NOT due to Disease Progression or Death.

# Savolitinib (AZD6094)

*Potential first-in-class selective c-Met inhibitor*

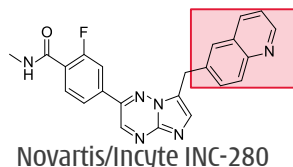
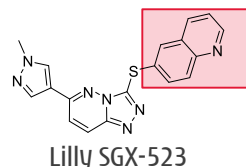
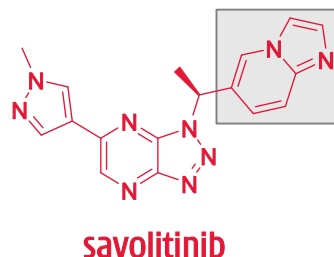
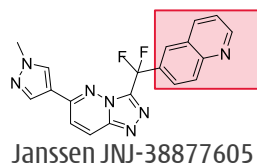
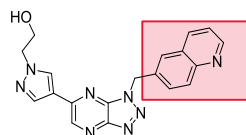
# Savolitinib (AZD6094)

## Potential first-in-class selective c-Met inhibitor

### 1. Strong potential to become first selective c-Met inhibitor approved.

- ✓ Clear clinical efficacy observed in **non-small cell lung ("NSCLC"), kidney, gastric and colorectal** cancers.
- ✓ Partnered with AstraZeneca - **key comp. advantages in NSCLC (Tagrisso® combo.) & molecular selection.**

### 3. Savolitinib design eliminates renal toxicity first generation of selective c-MET inhibitors encountered - >700 patients involved in clinical studies to date.



2-quinolinone metabolite in humans in 1<sup>st</sup>-gen c-Met compounds has dramatically reduced solubility and appeared to crystallize in the kidney resulting in obstructive toxicity.

### 2. c-Met is aberrant in many tumor settings. [3]

Indication	c-MET			New Cases (2015)	
	Amplification	Mutation	Over-Expression	Global	China
Gastric	10%	1%	41%	1,034,000	679,100
Lung	8-10% [1]	8%	67%	1,690,000	733,300
Head & Neck		11%	46%	740,000	135,000
Colorectal	10%		65%	1,477,000	376,300
Renal cell Carcinoma (Papillary)	40-70%	100% [2]		50,000	7,000
Renal cell Carcinoma (Clear cell)			79%	270,000	60,000
Esophagus	8%		92%	496,000	477,900
Prostate [4]			54-83%	1,100,000	60,300

### 4. AstraZeneca collaboration & 2016 amendment.

- \$20m received upfront (Dec 2011);
- \$120m in development/approvals milestones (\$25m received as of Jun 2018);
- Several hundred million in commercial milestones;
- Development costs: AZ pay 100% ex-China (excl. \$50m by Chi-Med) & 75% development cost in China (Chi-Med 25%);
- **14-18% tiered royalty ex-China [5]** & 30% flat rate China royalty on all product revenues.

[1] Range includes (i) approximately 4% of c-Met+ naïve non-small cell lung cancer patients and (ii) 10 - 30% of EGFR+ non-small cell lung cancer patients, which 15 to 20% develop EGFR+ tyrosine kinase inhibitor resistance pathway as c-Met+; [2] Hereditary papillary renal cell carcinoma only; [3] Company estimates considering Frost & Sullivan data, National Central Cancer Registry of China and publicly available epidemiology data; [4] By IHC, c-Met overexpression in 54% of lymph node disease and 83% of bone metastases. Varkaris et al, Expert Opin Investig Drugs. 2011 Dec; 20(12): 1677-1684; [5] Subject to approval in the papillary renal cell carcinoma (PRCC) indication and after total aggregate sales of savolitinib have reached \$5bn, the royalty will step down over a two-year period, to an ongoing royalty rate of 10.5% to 14.5%.

# Savolitinib - 1L NSCLC [1]

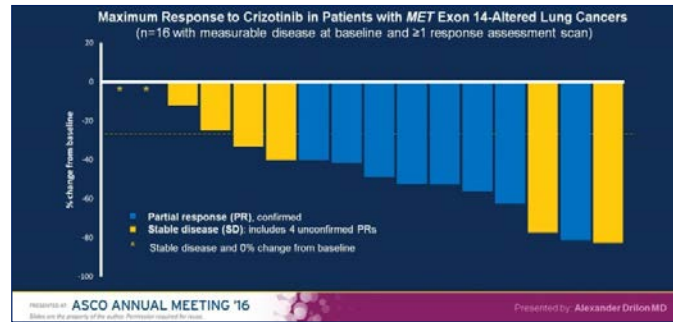
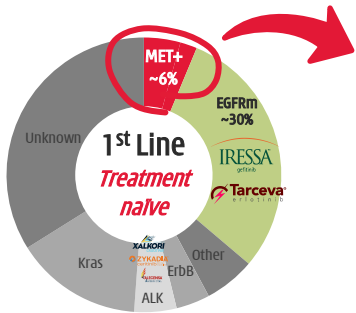


In regulatory dialogue - China Ph. II study now registration intent

1. Xalkori® is a **multi-kinase inhibitor with ALK, ROS1, & MET inhibition** - savolitinib is uniquely selective and **>10x** more potent against c-Met.

IC <sub>50</sub> (nM)	Savolitinib	Xalkori® (crizotinib)	Savolitinib vs. Xalkori®
EBC1 Viability	2	19	10X
EBC1 pMET	1	39	40X
293T MET (wild type)	7	79	11X
293T MET (EX14del)	9	140	16X

2. 1<sup>st</sup> line NSCLC - Xalkori® MET Exon14 del - 2016 ASCO - strong response (~50% ORR) but **>1/3 of responses not durable (4/12)** [2].

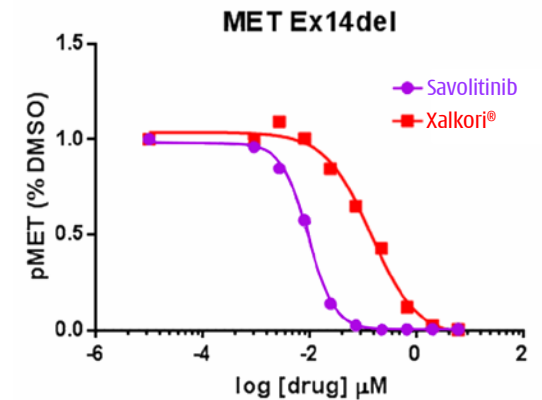


3. Multi-center retrospective analysis of 148 pts. w/ NSCLC MET Exon14 [3]

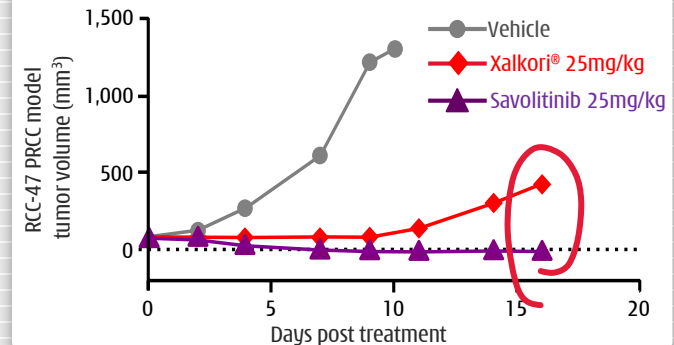
No. of pts	MET Exon14 skipping: Exposed to c-MET TKI	MET Exon14 skipping: Never exposed to c-MET TKI	Epidemiology of never-exposed to c-MET TKI	
	27	34	With concurrent c-MET amplification	Without concurrent c-MET amplification
Median OS	<b>24.6 months</b>	<b>8.1 months</b>	<b>5.2 months</b>	<b>10.5 months</b>

P=0.06

4. Savolitinib versus Xalkori® in MET Ex14del mutant cells [4] - **better target coverage.**



5. **Durable tumor cell suppression for savolitinib but not for Xalkori®** [5].



[1] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients;

[2] Drilon A, Abstract 108 Efficacy and safety of crizotinib in patients with advanced MET Exon 14-altered non-small cell lung cancer; [3] ASCO 2017, Abstract 8511, Mark M. Awad et al.; [4] Paik, P.K., et al., Response to MET inhibitors in patients with stage IV lung adenocarcinomas harboring MET mutations causing exon 14 skipping. Cancer Discov. 2015. 5(8): p. 842-9.; [5] Schuller AG et al. "Regression in Papillary Renal Cell Carcinoma Patient-Derived Xenograft Models". Clin Cancer Res 2015;21:2811-2819.

# Savolitinib - 2L EGFRm NSCLC

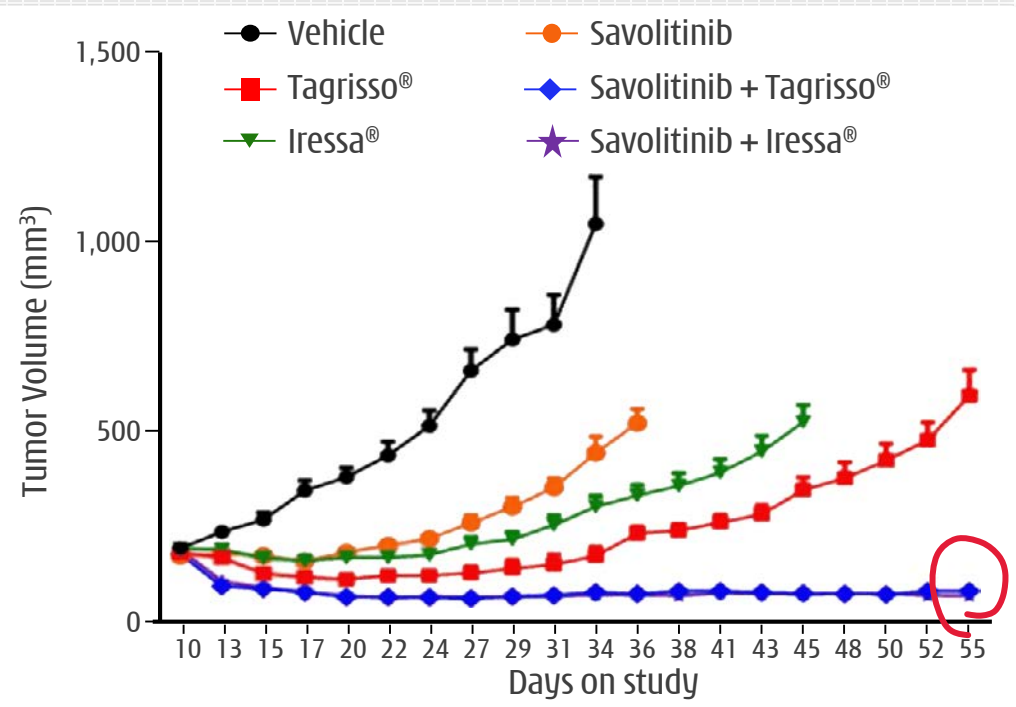
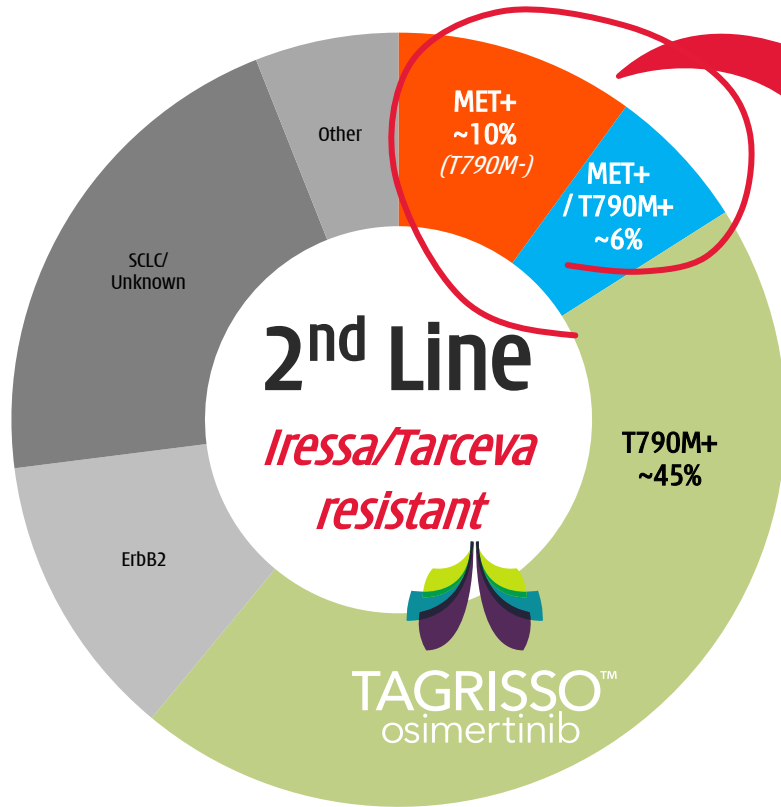
Very strong preclinical rationale for combination w/ EGFR-TKIs



1. 2<sup>nd</sup> Line NSCLC is the **fastest & most attractive indication for savolitinib** to go after. Also important unmet medical need and potential **Breakthrough Therapy** area.

2. Potential in **EGFR-TKI resistant NSCLC**:

- ✓ Must **shut down both EGFRm & MET** signaling pathways;
- ✓ **Prolonged tumor growth suppression** by combining savolitinib with Tagrisso® (osimertinib - EGFR/T790M) or Iressa® (gefitinib/EGFR) in **MET+ / T790M- patients**.



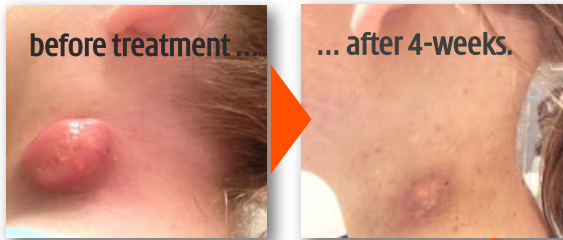
# Savolitinib - 2L NSCLC<sup>[1]</sup> combo w/



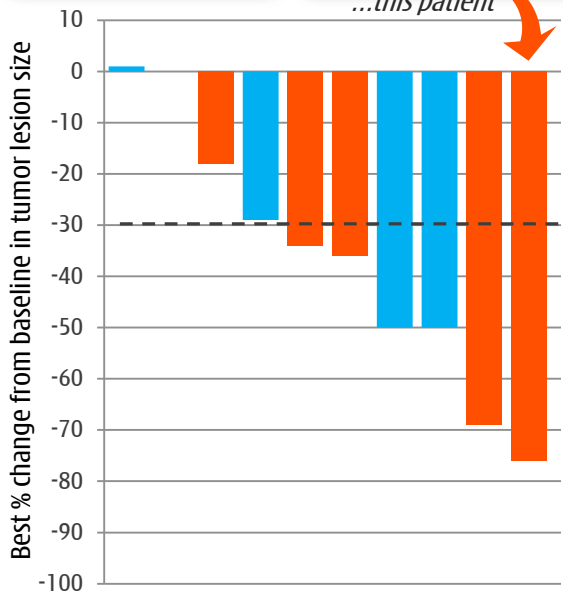
To initiate global registration study - with possible BTD dialogue

## TATTON A<sup>[2]</sup> - **signal...**

MET testing confirmation	Objective response rate, n (%)	Total (n = 10)
Local or Central	Confirmed PR <sup>[6]</sup>	<b>6 (60%)</b>



...this patient

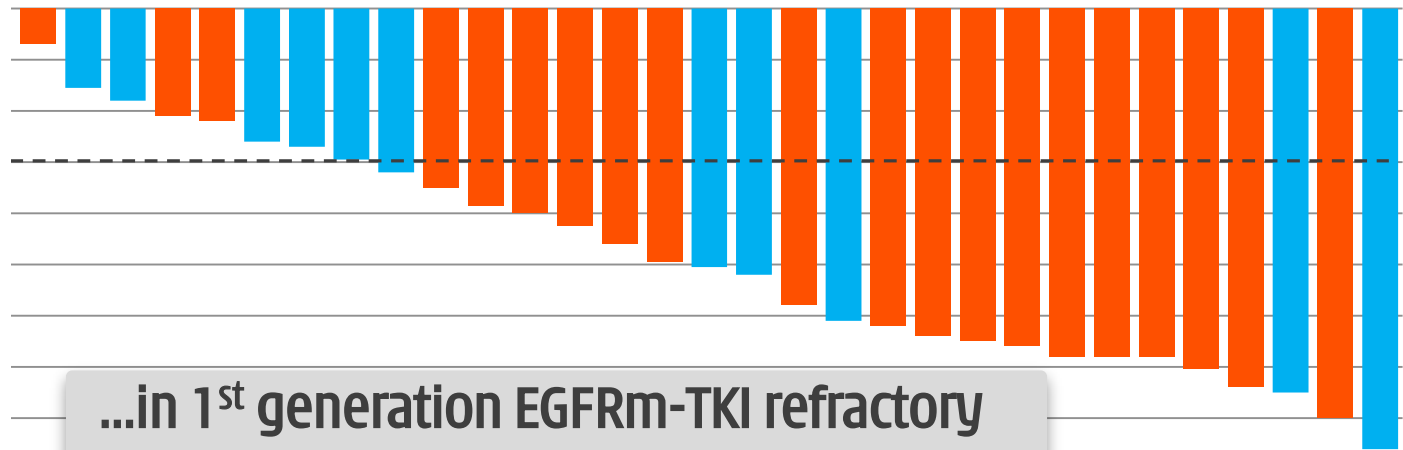


## ...TATTON B<sup>[3]</sup> - **...confirmation...** and BTD<sup>[4]</sup> potential?

MET testing confirmation	Objective response rate, n (%)	MET+ / T790M+ (n = 11)	MET+ (T790M-) (n = 23)	Total (n = 34)
Local or Central	Confirmed PR <sup>[6]</sup>	<b>6 (55%)</b>	<b>14 (61%)</b>	<b>20 (59%)</b>

		(n = 7)	(n = 15)	(n = 22)
Central *	Confirmed PR <sup>[6]</sup>	4 (57%)	8 (53%)	<b>12 (55%)</b>
	Stable Disease ≥6 weeks	3 (43%)	6 (40%)	<b>9 (41%)</b>
	Progressive Disease/death	0	1 (7%)	1 (5%)
	Not Evaluable	0	0	0 (0)
	DoR, months (range)	<b>9.7 (2.8*-9.7)</b>	NR (1.6*-5.9*)	NR (1.6*-9.7)

\* Centrally confirmed MET-amplification (fluorescence in-situ hybridization, MET gene copy ≥5 or MET/CEP7 ratio ≥2)<sup>[5]</sup>



...in 1<sup>st</sup> generation EGFRm-TKI refractory NSCLC patients **regardless of T790M status.**

# Savolitinib - 2L NSCLC<sup>[1]</sup> combo w/ IRESSA<sup>™</sup> gefitinib

Compelling in MET+ / T790M-, pivotal decision under discussion

IRESSA<sup>™</sup>  
gefitinib



## Savo / Iressa<sup>®</sup> combo in 1<sup>st</sup> gen. EGFRm-TKI refractory patients<sup>[2]</sup> ...outstanding response in MET+ / T790M-

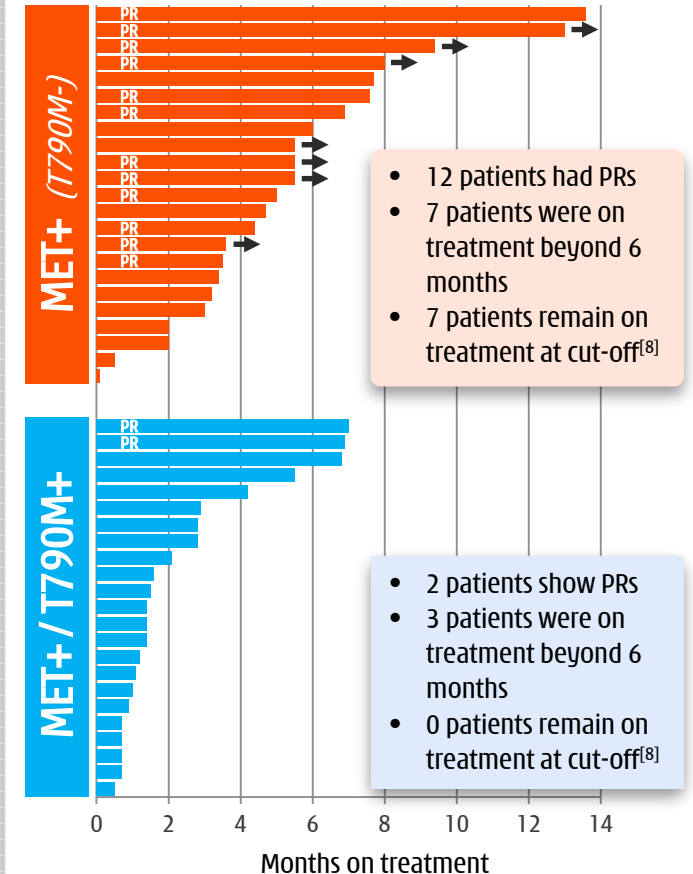
MET testing confirmation	Objective response rate, n (%)	MET+ / T790M+ (n = 23)	MET+ (T790M-) (n = 23)	MET+ / T790M unk. (n = 5)	Total (n = 51)
Central *	Confirmed PR <sup>[3]</sup>	2 (9%)	12 (52%)	2 (40%)	16 (31%)
	SD <sup>[4]</sup> ≥ 6 weeks	9 (39%)	7 (30%)	2 (40%)	18 (35%)
	PD <sup>[5]</sup> / death	7 (30%)	3 (13%)	0	10 (20%)
	Not Evaluable	5 (22%)	1 (4%)	1 (20%)	7 (14%)

## ...vs. TATTON B data (savo / Tagrisso<sup>®</sup> combo)<sup>[6]</sup>

MET testing confirmation	Objective response rate, n (%)	MET+ / T790M+ (n = 11)	MET+ (T790M-) (n = 23)	MET+ / T790M unk. (n = 0)	Total (n = 34)
Local or Central	Confirmed PR <sup>[3]</sup>	6 (55%)	14 (61%)	0	20 (59%)
Central *		(n = 7)	(n = 15)	(n = 0)	(n = 22)
	Confirmed PR <sup>[3]</sup>	4 (57%)	8 (53%)	0	12 (55%)
	SD <sup>[4]</sup> ≥ 6 weeks	3 (43%)	6 (40%)	0	9 (41%)
	PD <sup>[5]</sup> / death	0	1 (7%)	0	1 (5%)
	Not Evaluable	0	0	0	0 (0)

\* Centrally confirmed MET-amplification (fluorescence in-situ hybridization, MET gene copy ≥ 5 or MET/CEP7 ratio ≥ 2)<sup>[9]</sup>.

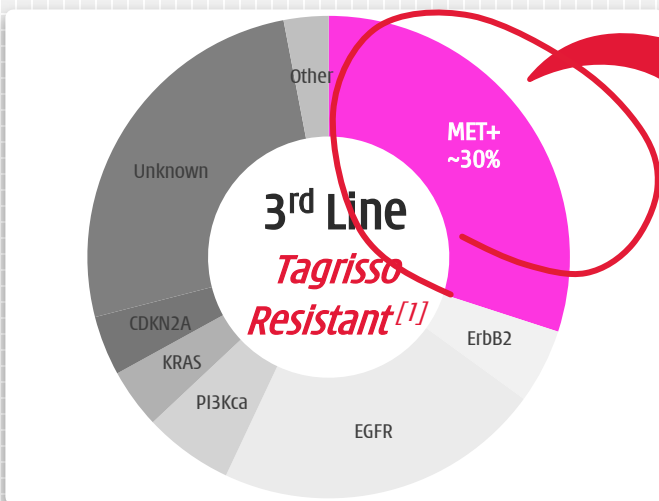
## ...Iressa<sup>®</sup> combo - ~6mo. DoR<sup>[7]</sup> in MET+ / T790M- patients



[1] EGFRm NSCLC; [2] WCLC 2017 Yang J-J, et al. A Ph.Ib Trial of savolitinib plus gefitinib for patients with EGFR-mutant MET-amplified advanced NSCLC; [3] PR = Partial Response; [4] SD = Stable Disease; [5] PD = Progressive Disease; [6] WCLC 2017 - Ahn M-J, et al. TATTON Phase Ib exp. cohort; [7] DoR = Duration of Response; [8] Aug 21, 2017; [9] On TATTON B, some local MET-status determined via IHC+3 in ≥ 50% of tumor cells.

# Savolitinib - 2L/3L NSCLC<sup>[1]</sup> - TAGRISSO<sup>™</sup> osimertinib resistant

## MET+ driven resistance in ~30% of patients

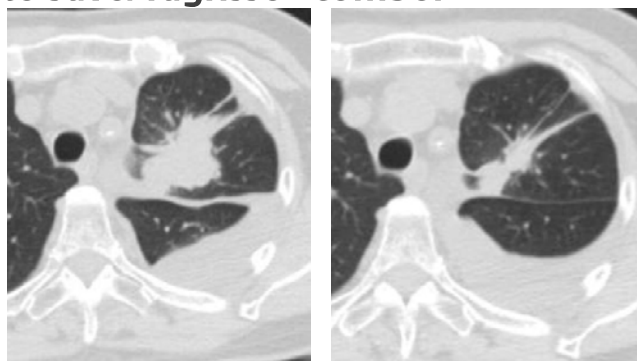


### Tagrisso<sup>®</sup> resistant tissue & ctDNA analysis<sup>[2]</sup>



Pt	EGFR mutation	# Prior Therapies	Prior 3 <sup>rd</sup> gen TKI	TISSUE (NGS, FISH)	PLASMA ctDNA (NGS)
1	L858R	1		MET amp, T790 WT	MET amp, T790M ND
2	Del19	1		-	T790M ND
3	Del19	2	Y	-	T790M ND
4	L858R (de novo T790M)	2	Y	MET amp, EGFR amp T790M (germline)	-
5	L858R	3	Y	T790wt, EGFR amp	T790M ND
6	L858R	4	Y	T790 WT	T790M ND
7	Del19	3	Y	-	T790M ND
8*	Del19	3		T790M/C797S	T790M/C797S
9	L858R	4	Y	T790 WT	-
10	Del19	3	Y	-	PIK3CA E545K, PIK3CA amp, T790M ND
11	Del19	2	Y	MET amp, EGFR amp, T790 WT	T790M ND
12	Del19	2	Y	-	T790M/C797S
13	Del19	9		T790 WT	-
14	Del19	2	Y	T790 WT	T790M ND
15	Del19	1		T790 WT	FGFR1 D60N, FGFR1 amp, T790M ND
16	L858R	2		MET amp, T790 WT	MET, EGFR amp, T790M ND
17	L858R	3	Y	T790 WT	T790M ND
18	Del19 (de novo T790M)	3		SCLC, T790 WT	T790M ND, EGFR amp
19	Del19	3	Y	T790 WT	T790M/C797S, MET amp, EGFR amp
20	L858R	2		MET amp, EGFR amp, T790 WT	-
21	L858R	3		-	T790M/C797S, EGFR amp
22*	L858R	1		MET amp, T790 WT	-
23	Del19	4	Y	-	T790M/C797S

**3 out of 3 MET+ patients responded to savo/Tagrisso<sup>®</sup> combo.**



LUL Mass Pre-Treatment      6 wks. on savo/Tag. Treatment

(-) Testing not performed; EGFR - Epidermal Growth Factor Receptor; TKI- Tyrosine Kinase Inhibitor; amp - amplification; WT - wild type; ND - not detected

[1] Based on rocletinib/Tagrisso data published at 2016/2017 ASCO; [2] In xenograft model H820, with EGFRm, T790M+ and MET CN gain. D'Cruz CM et al; #761 Preclinical data for changing the paradigm of treating drug resistance in NSCLC:

Novel combinations of AZD6094, a selective MET inhibitor, and AZD9291 an irreversible, selective (EGFRm and T790M) EGFR TKI; American Association of Cancer Research Annual Meeting; April 19, 2015.

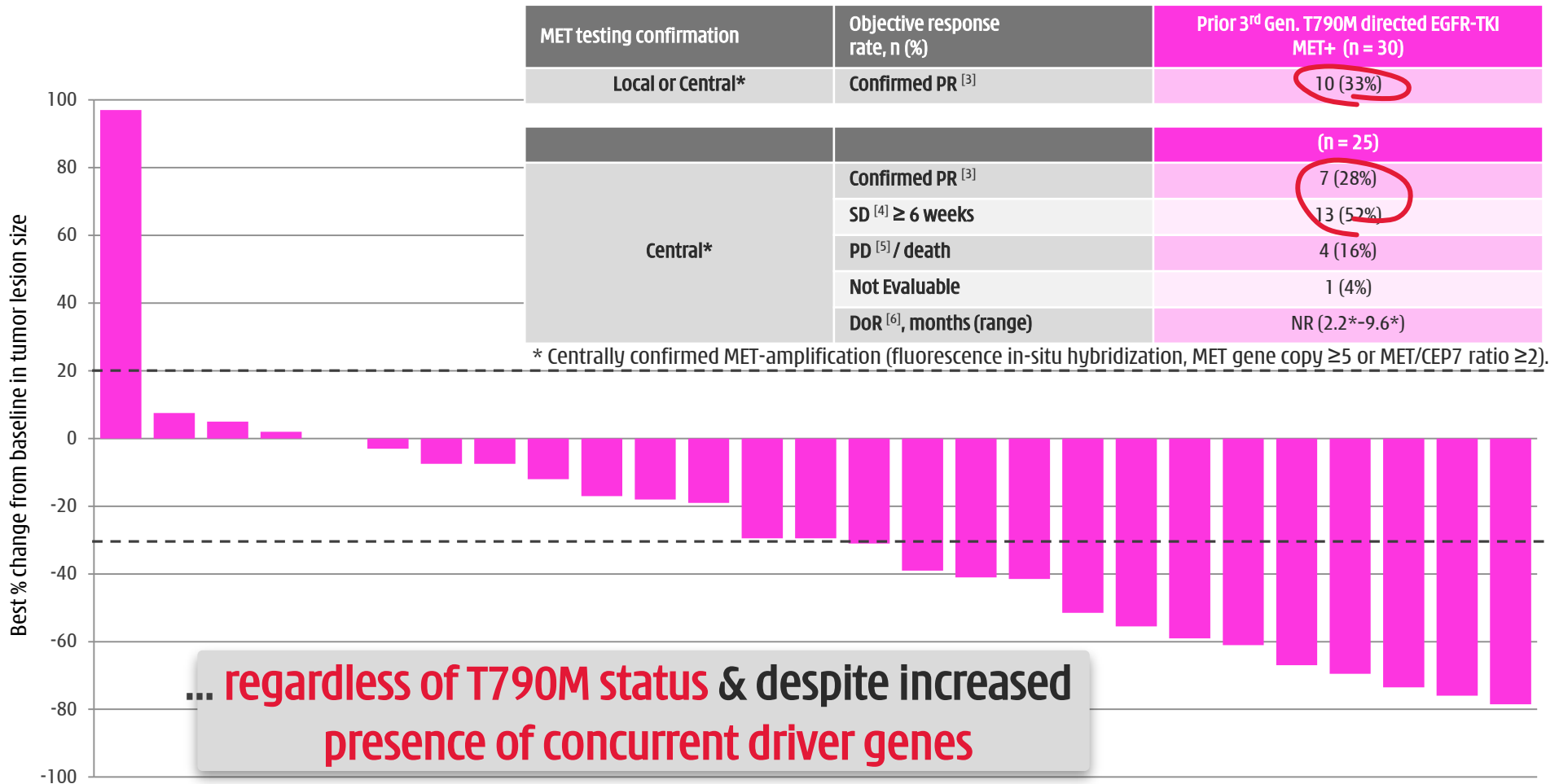


# Savolitinib - 2L/3L NSCLC<sup>[1]</sup> combo w/



To initiate global registration study in late 2018

## ...TATTON B<sup>[2]</sup> - ...promising efficacy in MET+ Tagrisso failure patients...



[1] EGFRm NSCLC; [2] WCLC 2017 - Ahn M-J, *et al.* TATTON Phase Ib expansion cohort; Waterfall plot based on evaluable patients (n=30): all patients dosed and with on-treatment assessment or discontinuation prior to first tumour assessment; Data cut-off 31 Aug 2017; [3] PR = Partial Response; [4] SD = Stable Disease; [5] PD = Progressive Disease; [6] DoR = Duration of Response.

# Tolerability - savo plus



or



# TATTON D - 300mg QD dose potentially support long-term use

## Efficacy / Tolerability analysis in ≥ 2<sup>nd</sup>-Line NSCLC

US FDA Approval Date	Treatment / Control arms	Disease setting	n	Efficacy		Discontinuations as % Enrolled		
				ORR	Median PFS (mo.)	Due to AE	Withdrawn / Other	Total [5]
<b>Non-Small Cell Lung Cancer -- Treatment arms</b>								
30-Mar-17	Tagrisso® (osimertinib)	2L EGFRi-refractory T790M+ NSCLC (AURA3)	279	71%	10.1	6%	6%	13%
29-Apr-14	Zykadia® (ceritinib)	2L ALK+ NSCLC after Xalkori (single arm)	163	56%	6.9	10%	10%	20%
12-Dec-14	Cyramza® (ramucirumab) + Taxotere®	2L NSCLC after plat-chemo	624	23%	4.5	15%	21%	37%
24-Oct-16	Keytruda® (pembrolizumab) 2mg/kg	2L PD-L1+ (TPS≥1%) NSCLC after plat-chemo (KEYNOTE-010)	345	18%	3.9	10%	26%	37%
2-Oct-15	Keytruda® (pembrolizumab) 10mg/kg	2L PD-L1+ (TPS≥1%) NSCLC after plat-chemo (KEYNOTE-010)	346	18%	4.0	9%	27%	36%
9-Oct-15	Opdivo® (nivolumab)	2L NSCLC after plat-chemo	292	19%	2.3	15%	4%	20%
4-Mar-15	Opdivo® (nivolumab)	2L squ. NSCLC after plat-chemo	135	20%	3.5	12%	8%	20%
<b>Non-Small Cell Lung Cancer -- Control arms (aggregate / weighted average)</b>								
	Chemo doublet (platinum + pemetrexed)	2L NSCLC (AURA3)	136	31%	4.4	11%	17%	27%
	Taxotere® (docetaxel)	2L NSCLC (REVEL; KEYNOTE-010; Opdivo x2)	1,391	12%	3.5	13%	22%	36%
<b>Savolitinib</b>								
	savolitinib 600mg QD monotherapy [3]	All-lines Papillary RCC -- FOR REFERENCE ONLY	109 [1]	18%	6.2	9%	5%	14%
	savolitinib 600mg QD + Iressa® (gefitinib) [4]	≥2L EGFRm+ c-MET+ T790M- NSCLC after 1 <sup>st</sup> -gen EGFR TKI (expansion)	51 [2]	52%	ND	20%	14%	33%
	savolitinib 600mg QD + Tagrisso® [4]	≥2L EGFRm+ c-MET+ T790M-/± NSCLC after 1 <sup>st</sup> -gen EGFR TKI (TATTON B)	34	59%	ND	30%	3%	33%
	savolitinib 600mg QD + Tagrisso® [4]	≥3L EGFRm+ c-MET+ NSCLC after 3 <sup>rd</sup> -gen EGFR TKI (TATTON B)	30	33%	ND			

[1] PRCC Phase II - Efficacy data from MET+ patients (n=44), discontinuation data from late 2017 data cut-off; Tolerability data from all patients (n=109); [2] TATTON Study - Efficacy data for noted molecular subsets; Tolerability data from all patients (n=64); [3] September 2017 Journal of Clinical Oncology; [4] 2017 World Conference on Lung Cancer; [5] Total discontinuations = Discontinuations NOT due to Disease Progression or Death; ND = Not Disclosed.

# Safety - savolitinib plus

**IRESSA™**  
gefitinib

or

**TAGRISSEO™**  
osimertinib



# Adverse event profiles of combinations - manageable & tolerable

	IPASS Phase III 1 <sup>st</sup> -Line EGFRm NSCLC			FLAURA Phase III 1 <sup>st</sup> -Line EGFRm NSCLC		AURA3 Phase III 2 <sup>nd</sup> -Line EGFRm NSCLC		
Grade ≥3 AEs, Preferred term, n (%)*	IPASS Iressa® (N=607)	IPASS carbo. + Taxol® (N=589)	≥ 2 <sup>nd</sup> -Line [2] Savo + Iressa® (N=51)	Tagrisso® (N=279)	Iressa® or Tarceva® (N=277)	Tagrisso® (N=279)	Chemo-doublet (plat. + pemetrex.) (N=136)	≥ 2 <sup>nd</sup> -Line [1] Savo + Tagrisso® (N=66)
<b>Any Grade ≥3 AE</b>	<b>29% (Gr. 3-4)</b>	<b>61% (Gr. 3-4)</b>	<b>17 (33%)</b>	<b>94 (34%)</b>	<b>124 (45%)</b>	<b>63 (23%)</b>	<b>64 (47%)</b>	<b>33 (50%)</b>
Vomiting	1 (<1%)	16 (3%)		0	4 (1%)	1 (<1%)	3 (2%)	5 (8%)
Rash or acne	19 (3%)	5 (1%)		3 (1%)	19 (7%)	2 (1%)		4 (6%)
AST/ALT increase			8 (16%)	3 (1%)	37 (13%)	6 (2%)	2 (2%)	4 (6%)
Nausea	2 (<1%)	9 (1%)	1 (2%)	0	0	2 (1%)	5 (4%)	3 (5%)
Decreased appetite				7 (3%)	5 (2%)	3 (1%)	4 (3%)	3 (5%)
Fatigue				2 (1%)	2 (1%)	3 (1%)	1 (1%)	3 (5%)
Neutropenia	22 (4%)	387 (67%)				4 (1%)	16 (12%)	3 (5%)
ALP increased			11 (22%)					
Neurotoxic effects	2 (<1%)	29 (5%)						
Anemia	13 (2%)	61 (11%)		3 (1%)	3 (1%)	2 (1%)	16 (12%)	
Leukopenia	9 (1%)	202 (35%)					5 (4%)	
Thrombocytopenia						1 (<1%)	10 (7%)	

Sources: [1] TATTON B - Figures where any grade AE ≥10% patients. Ahn M-J, et al. Abstract #8985. Presented at the World Lung Cancer Congress (WCLC) 2017, Japan, October 2017;

[2] Phase Ib/II study - Figures where any grade AE ≥10% patients. Yang J-J, et al. Abstract #8995. Presented at WCLC 2017, Japan, October 2017.

AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase.

# MET+ PRCC - unmet medical need

## 1. No treatment choices for non-ccRCC patients.

### Approved therapies in RCC [3]

*Good efficacy in ccRCC; Multiple treatment options*

FIRST LINE - clear-cell RCC [4]	ORR	mPFS	mOS
Placebo (avg. multiple studies)	~2%	~3.5	~15.0
Interferon- $\alpha$	6%	5.0	21.8
Nexavar <sup>®</sup> (VEGFR, multi-kinase SM) (avg. multiple studies)	~12%	~6.0	~21.0
Sutent <sup>®</sup> (VEGFR, multi-kinase SM) (avg. multiple studies)	~28%	~10.5	~27.0
Votrient <sup>®</sup> (VEGFR, multi-kinase SM)	31%	10.5	28.4

### SECOND LINE - clear-cell RCC

Placebo (avg. multiple studies)	~0%	~2.0	~14.0
Afinitor <sup>®</sup> (mTOR) (METEOR)	3%	3.9	16.5
Afinitor <sup>®</sup> (mTOR) (CheckMate025)	5%	4.4	19.6
Inlyta <sup>®</sup> (VEGFR, multi-kinase SM)	23%	8.3	20.1
Opdivo <sup>®</sup> (PD-1 mAb) (CheckMate025)	25%	4.6	25.0
Cabometyx <sup>®</sup> (VEGFR/MET, multi-kinase SM) (METEOR)	17%	7.4	21.4

### Nothing approved in non-ccRCC

*NCCN guideline - "Patients should enter clinical trials"*

FIRST LINE - non clear-cell RCC	ORR	mPFS	mOS
Sutent <sup>®</sup> (VEGFR, multi-kinase SM) [4]	9%	6.1	16.2
Afinitor <sup>®</sup> (mTOR) [4]	3%	4.1	14.9

SECOND LINE - non-clear-cell RCC	ORR	mPFS	mOS
Sutent <sup>®</sup> (VEGFR, multi-kinase SM) [4]	10%	1.8	na
Afinitor <sup>®</sup> (mTOR) [4]	9%	2.8	na

## 2. RCC est. ~\$3.3 bln. market by 2020 [1]

Clear-cell RCC  
(~\$2.7b)  
~80% of RCC  
~ 270k new patients/yr.[2]

Non-Clear-cell RCC  
(~\$0.6b)  
~20% of RCC  
~ 70k new patients/yr.[2]

## 3. Two crucial questions:

MET+  
Papillary RCC  
(~\$0.2-0.3b)  
~7% of RCC  
~ 25k new patients/yr.[2]

MET-  
Papillary RCC  
(~\$0.2-0.3b)  
~7% of RCC  
~ 25k new patients/yr.[2]

Other non-ccRCC  
(~\$0.1-0.2b)  
~5% of RCC  
~ 20k new patients/yr.[2]

**Question 1:** Does savolitinib provide meaningful benefit to patients w/ MET+ PRCC?

**Answer:** Phase II data (next page)

**Question 2:** Is MET+ status predictive of worse outcome (PFS/OS) in PRCC patients?

**Answer:** >200 pt. PRCC Molecular Epidemiology Study

[1] Transparency Market Research, March 2015 - RCC (excl. non-RCC Kidney Cancer) global market size; [2] Frost & Sullivan, March 2016; [3] NCCN Guideline for kidney cancer. Version 3.2016, 05/26/16, RCC = renal cell carcinoma;

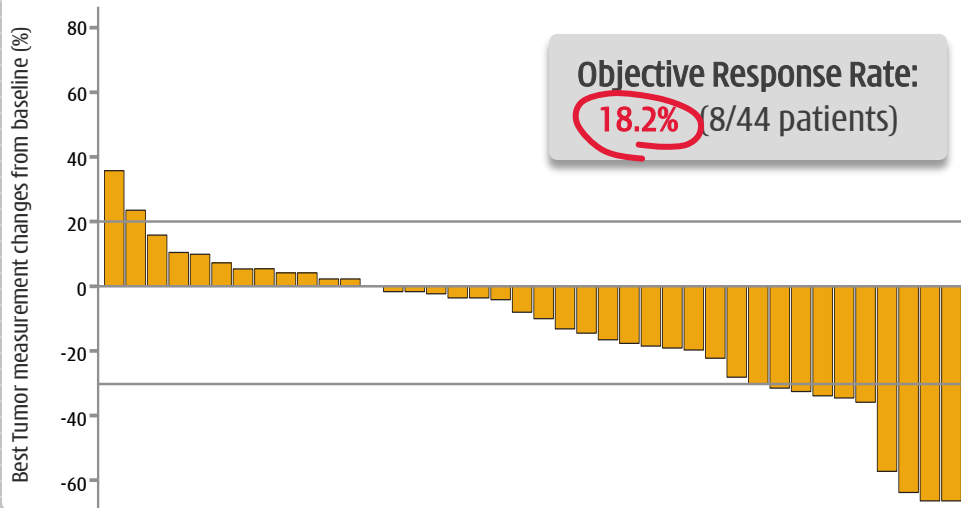
[4] ORR = Objective Response Rate, mPFS = median Progression Free Survival, mOS = median Overall Survival

# Savolitinib - PRCC Phase II

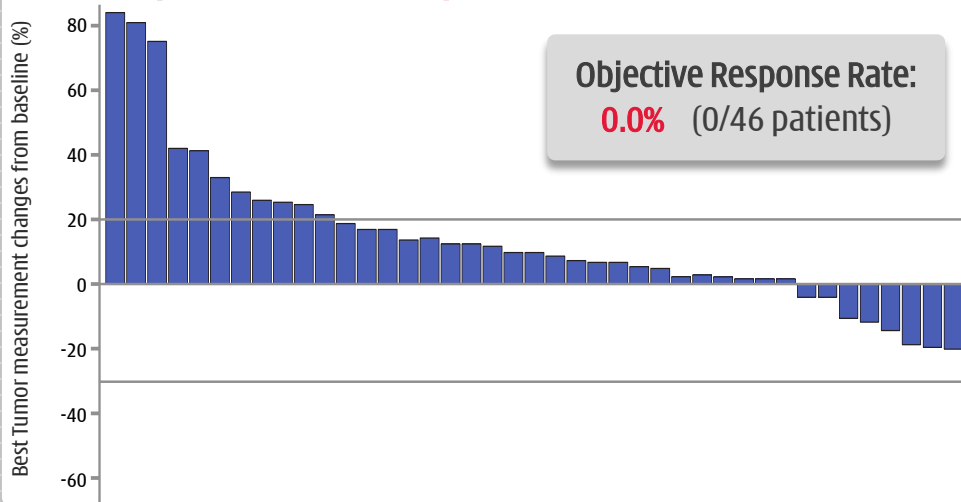
## Clear efficacy & durable response in MET+ PRCC patients



### 1. Savolitinib clear ORR benefit in MET+ patients.



### 2. MET- patients - no response to savo.



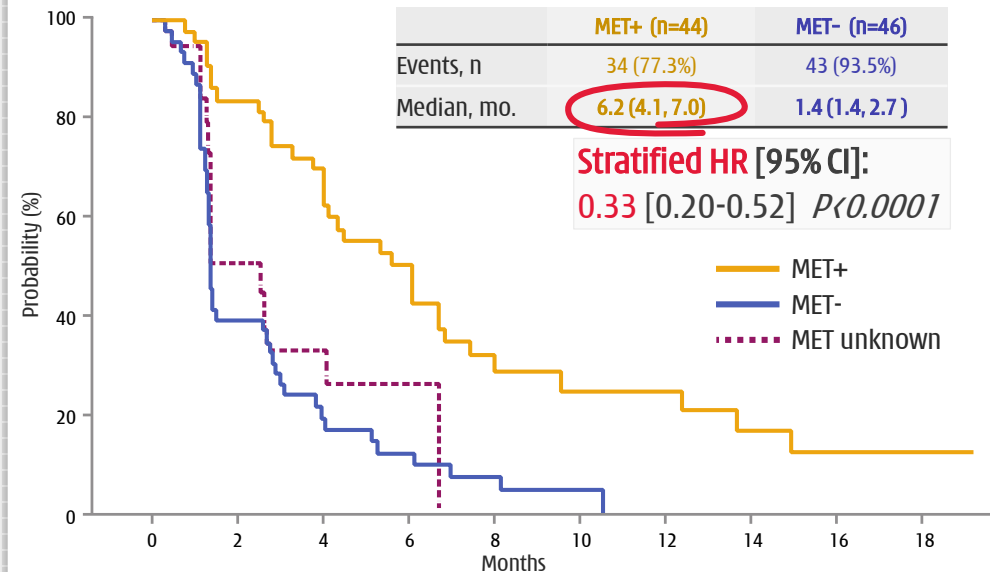
### 3. Disease Control Rate ("DCR") - big advantage in MET+ with **DCR 73.2%** vs. MET- **28.2%**.<sup>^</sup>

Tumor responses in the overall treatment population and by MET status

RECIST response, n (%)	MET+ (n=44)	MET- (n=46)	MET unknown (n=19)	Total (n=109)
Partial Response <sup>†</sup>	8 (18.2%)*	0 (0.0%)	0 (0.0%)	8 (7.3%)
Stable Disease	22 (50.0%)	11 (23.9%)	5 (26.3%)	38 (34.9%)
Progressive Disease	11 (25.0%)	28 (60.9%)	9 (47.3%)	48 (44.0%)
Not Evaluable	3 (6.8%)	7 (15.2%)	5 (26.3%)	15 (13.8%)

\* P=0.002 versus MET-independent subgroup (Fisher exact test). Responses assessed according to RECIST version 1.1. <sup>†</sup> Unconfirmed responses excluded. <sup>^</sup> Evaluable patients.

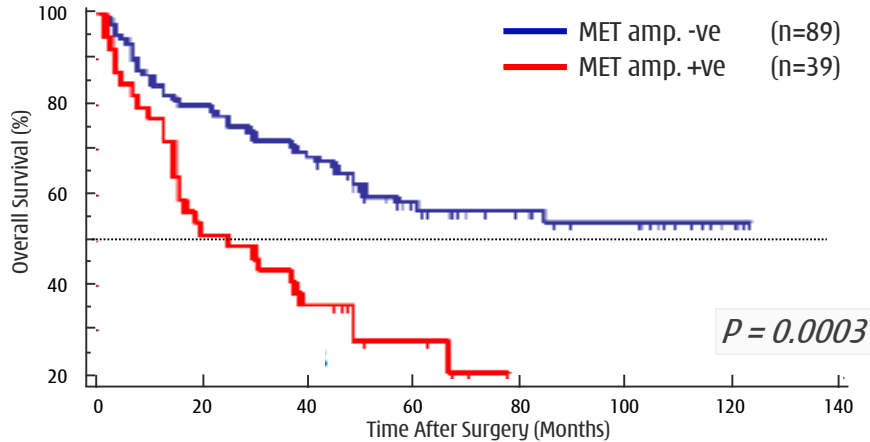
### 4. Median PFS - big advantage in MET+ patients.



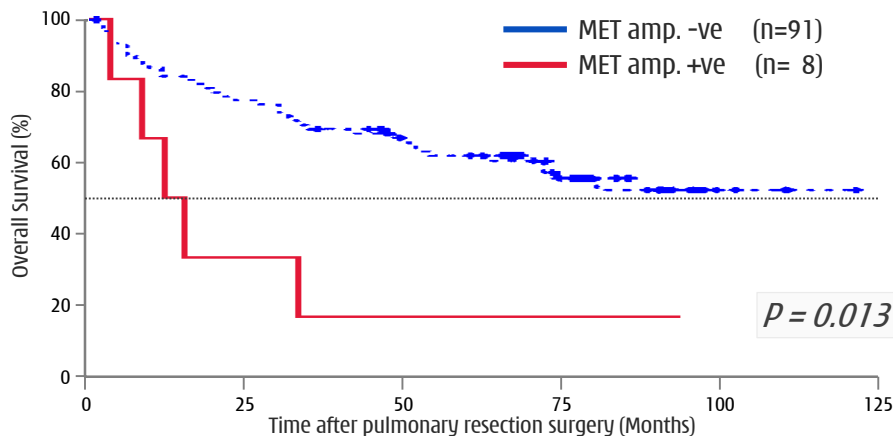
# MET-driven disease

A predictor of very poor patient outcome in many cancers

## 1. Gastric cancer MET-driven ...far worse survival.<sup>[1]</sup>



## 2. SCC NSCLC MET-driven ...far worse survival.<sup>[2]</sup>



## 3. PRCC Molecular Epidemiology Study ("MES") Plan:

- ➔ A pooled analysis of historical data - to correlate MET-driven PRCC status with documented historical treatment outcomes.
- ➔ 3 collaborations - GETUG<sup>[3]</sup> (France); IMDC<sup>[4]</sup> (N. America, EU, Asia, New Zealand); & Asan GU (Korea). Total >200 patient data.
- ➔ Timing - MES currently underway **Results expected late 2018.**



ASAN Medical Center

IMDC

PRCC Patient Data (n >200)

- ➔ Tissue samples for MET testing
- ➔ Medical records - treatment history/outcomes

## 4. How we will use the MES data set?

- ➔ Possible Breakthrough Therapy discussion - with clear evidence that c-MET-driven PRCC has far worse treatment outcome/survival than MET-independent.
- ➔ Clarity on PFS/OS treatment outcome of MET-driven patients - how do MET-driven PRCC patients (vs. MET-independent) respond to sunitinib and other approved RCC therapies.

[1] c-MET amplification: gene copy number of  $\geq 4$ . J Shi et al. Frequent Gene Amplification Predicts Poor Prognosis in Gastric Cancer. *Int. J. Mol. Sci.* 2012, 13, 4714-4726; [2] SCC NSCLC = squamous cell carcinoma non-small cell lung cancer. (~20-30% of NSCLC) -- c-MET gene amplification: >15 copies in >10% of tumor cells with 4-10 copies in a gene cluster. H Go et al. High MET Gene Copy Number Leads to Shorter Survival in Patients with Non-Small Cell Lung Cancer. *J. Thorac. Oncol.* 2010, 5, 303-313.; [3] GETUG = Groupe d'Étude des Tumeurs Urogénitales; [4] IMDC = International Metastatic Renal Cell Carcinoma Database Consortium.

# Savolitinib - PRCC Phase II

Safe & very well tolerated -advantage over other RCC TKIs [7]



		PRCC PHASE II	COMPARZ PHASE III [1]		METEOR PHASE III [2]		SINGLE-ARM PHASE III [3]
		Savolitinib 1L/2L (n=109)	Sunitinib 1L (n=548)	Pazopanib 1L (n=554)	Cabozantinib 2L (n=331)	Everolimus 2L (n=322)	Sunitinib 2L (n=106)
MSKCC Risk Group	Favorable	14%	27%	27%	45%	46%	58%
	Intermediate	45%	59%	58%	42%	41%	42% <sup>[6]</sup>
	Poor	9%	9%	12%	12%	13%	0%
	Missing	32%	4%	3%	0%	0%	0%
Number of prior systemic therapies	0	55%	100%	100%	0%	0%	0%
	1	23%	0%	0%	71%	70%	100%
	≥2	22%	0%	0%	29%	30%	0%
Grade ≥3 AEs:	Any AE	47%			68%	58%	
	Any treatment-related AE [4]	19%	77% <sup>[5]</sup>	76% <sup>[5]</sup>			
All Grade ≥3 AEs with ≥5% incidence (AND selected savolitinib AEs for comparison)	Hypertension	0%	15%	15%	15%	3%	6%
	Fatigue	2%	17%	11%	9%	7%	11%
	Hand-foot-syndrome	0%	12%	6%	8%	<1%	7%
	Diarrhea	0%	8%	9%	11%	2%	
Hematologic Abnormalities Grade ≥3 AEs with ≥5% incidence:	Neutropenia	0%	20%	5%	0%	0%	16%
	Thrombocytopenia	0%	24%	4%	0%	0%	6%
	Lymphocytopenia	0%	14%	5%	0%	0%	
	Leukopenia	0%	6%	1%	0%	0%	
Lab Abnormalities Grade ≥3 AEs with ≥5% incidence:	Anemia	<1%	7%	2%	5%	16%	6%
	Increased ALT	5%	4%	17%	2%	<1%	
	Increased AST	3%	3%	12%	2%	<1%	
	Hypophosphatemia	0%	9%	4%	4%	2%	
	Hyponatremia	3%	7%	7%	0%	0%	
Tolerability	Dose reduction due to AE:	13%	51%	44%	62%	25%	
	Treatment discontinuation due to any AE [8]:	8%	20%	24%	12%	11%	11%

Better safety data despite higher risk patient population:  
 ✓ Only 14% "favorable" vs. 27-58%.

Superior safety profile vs. other TKIs - Most ≥3 G3 AEs ≈ 0-2%:  
 ✓ Hypertension: 0% vs. 6~17%.  
 ✓ Fatigue: 2% vs. 6~12%.  
 ✓ Diarrhea: 0% vs. ~10%.  
 ✓ Anemia: <1% vs. 7~16%.  
 ≈ ALT/AST Increase: 3-5% vs. 0~17%.  
 ✓ Other Lab Abnorm: 0% vs. ≤9%.

Highly tolerable vs. other TKIs:  
 ✓ Discontinued: 8% vs. 10~24%.  
 ✓ Dose reduction: 13% vs. 44-62%.

[1] RJ Motzer et al, *Pazopanib versus Sunitinib in Metastatic Renal-Cell Carcinoma*, N Engl J Med 369:8, Aug 22, 2013; [2] TK Choueiri et al, *Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR)*, Lancet Oncol.17;7, Jun 5, 2016; [3] RJ Motzer et al, *Sunitinib in Patients with Metastatic Renal Cell Carcinoma*, JAMA 295:21 Jun 7, 2006; [4] As assessed by investigator; [5] Includes Grade 5 AEs; [6] Includes Intermediate & Poor. TRAES = Treatment-Related Adverse Events; [7] RCC = Renal Cell Carcinoma; [8] Early 2017 ASCO Genitourinary Cancers Symposium data cut-off.

# Savolitinib - Gastric cancer

A major problem in east Asia - Japan, South Korea & China

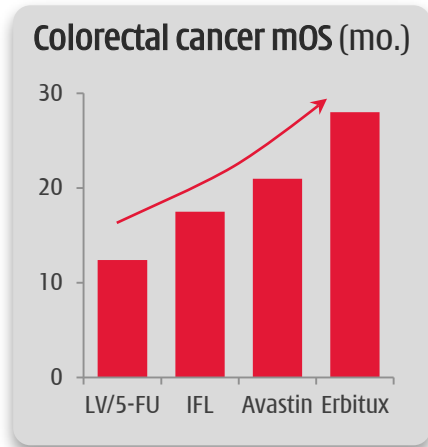
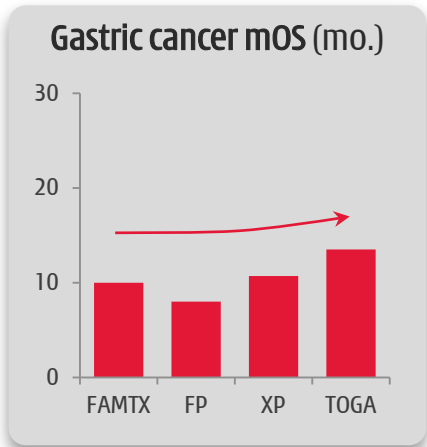


1. Gastric (stomach) cancer is the 5<sup>th</sup> most common cancer globally - **723,000 deaths/year**.

	Est. Age Standardised Rates (cases/100,000)	New cases ('000)	Deaths ('000)	5-year Prevalence ('000)
World	17.0	952	723	1,538
South Korea	41.8	22	17	32
Japan	29.9	38	29	56
China	22.7	<b>405</b>	325	594
EU-28	9.0	82	58	119
USA	6.8	21	12	32

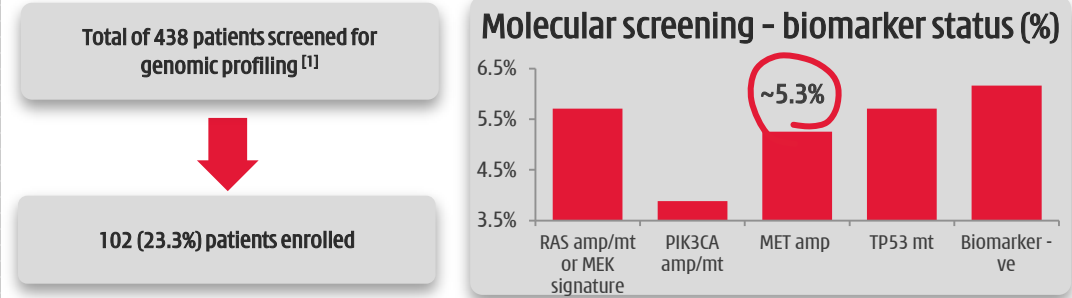
Jeeyun Lee, AACCR 2016; IARC, WHO 2012; Jung KW, Cancer Research Treatment 2013; World Cancer Research Fund International.

2. **Little progress in gastric cancer<sup>[2]</sup>** in improving overall survival ("OS") in first-line palliative setting.

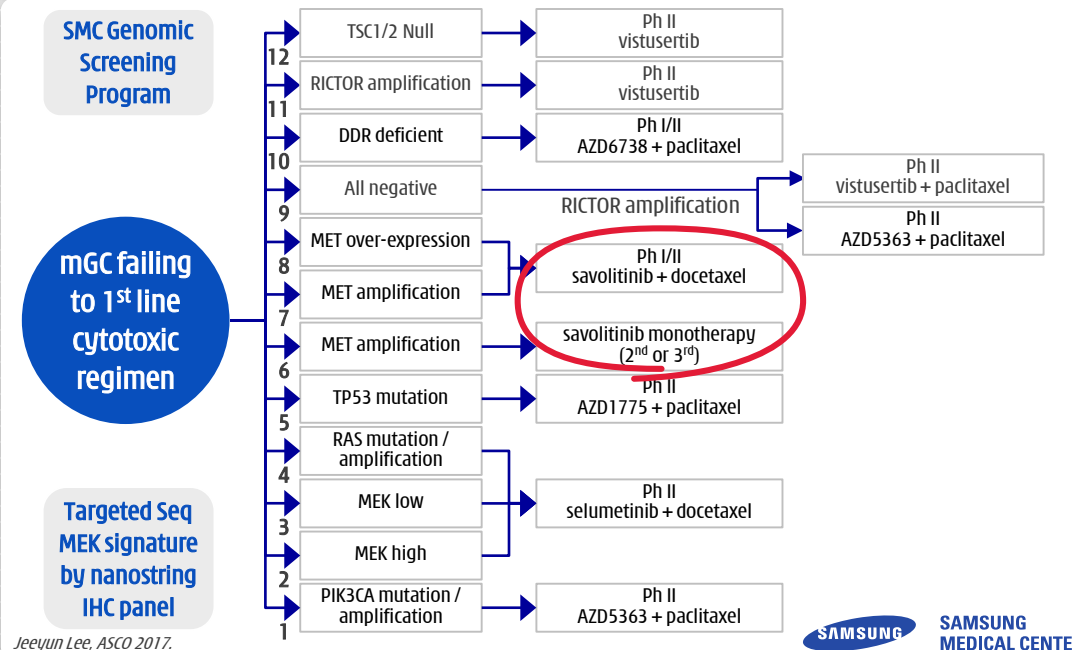


Jeeyun Lee, AACR 2016; Mayer RJ, J Clin Oncol 2015.

3. **VIKTORY - umbrella trial** in gastric cancer (*South Korea*).



Jeeyun Lee, ASCO 2017



Jeeyun Lee, ASCO 2017.



[1] Since June 2014; [2] FAMTX = 5-FU + doxorubicin + methotrexate; FP = cisplatin + 5-FU; XP = capecitabine + cisplatin; TOGA = trastuzumab + chemo; LV/5-FU = leucovorin + 5-FU; IFL = irinotecan + 5-FU + leucovorin.





# Fruquintinib

*Highly selective anti-angiogenesis inhibitor -  
Designed to be best-in-class*



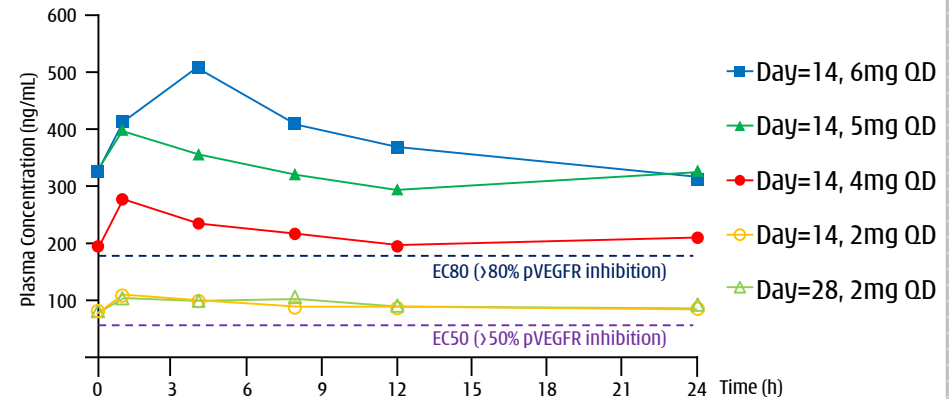
# Fruquintinib - 24hr full target coverage

The most selective VEGFR inhibitor in clinical trials globally <sup>[1]</sup>

## 1. Fruquintinib China NDA submission June 2017 - regulatory approval process almost complete.

- ✓ Validation of R&D approach - designed to only inhibit VEGFR1,2,3, facilitating **full target coverage & combinations**.
- ✓ **Pivotal Phase III in 3L CRC met all endpoints - NDA submitted Q2 2017.**
- ✓ **Pivotal Phase III in 3L NSCLC fully enrolled - top-line results Q4 2018.**
- ✓ **Pivotal Phase III Taxol® combo in 2L gastric cancer - initiated Oct 2017.**
- ✓ **Phase II Iressa® combo in 1L EGFRm+ NSCLC - early data at WCLC 2017.**
- ✓ **Phase I in solid tumors in US - initiated Q4 2017.**
- ✓ China GMP **facility built and certified** to support launch.

## 2. Only inhibits VEGFR - limits off-target toxicity & allows for full & sustained target inhibition.



## 3. Selectivity and potency superior to competitors' drugs.

	Sutent® (sunitinib)	Nexavar® (sorafenib)	Stivarga® (regorafenib)	Tivozanib	Fruquintinib
Kinase profile	VEGFR1,2,3, PDGFRβ, FLT3, CSF-1R, c-Kit, Ret	RAF, VEGFR2, PDGFRβ, Flt3, c-Kit, FGFR1	VEGFR1,2,3, Raf, Ret, PDGFR, c-Kit	VEGFR1,2,3, BRK, PDGFRα, PDGFRβ, c-Kit, Tie2, EphB2	VEGFR1,2,3
AUC at ED50/ED60 in mouse (ng/mL*hr)	2,058	25,473	na	1,640	898
MTD in human (mg/day)	50, qd	400, bid	160, qd	1.5, qd	4, qd; 6, 3wk/1wk
AUC, 0~24h at Steady state MTD (ng/mL*hr)	592	47,780 x2 (D28)	58,270 (D21)	1,180 (D28)	5,000~6,000 (D28)
Efficacy in Phase I	22 patients PR: 4 (18%), DCR: 27%	45 patients [2] PR: 1 (2%), DCR: 58%	53 patients PR: 3 (6%), DCR: 66%	37 evaluable patients PR: 1 (3%), DCR: 51%	34 evaluable patients PR: 13 (38%), DCR: 82%

[1] Among small molecule tyrosine kinase inhibitors and to the best of Chi-Med's knowledge; [2] (≥100 mg bid); PR = Partial Response; DCR = Disease Control Rate.

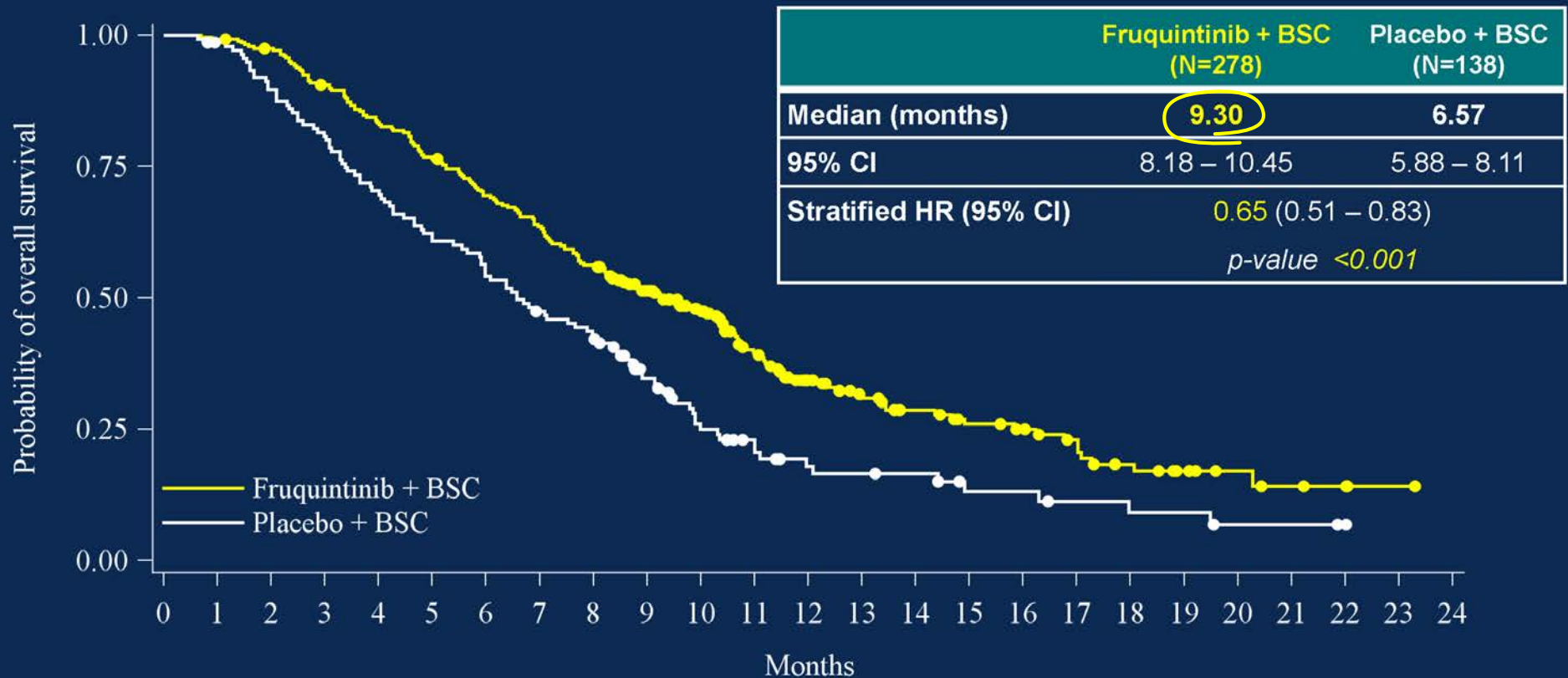
# Fruquintinib - 3L colorectal cancer

Best-in-class efficacy/safety - Ph.III FRESCO data ASCO 2017 [1]



## Overall Survival (Primary Endpoint)

FRESCO clearly succeeded in meeting the primary efficacy endpoint of OS



[1] ASCO = American Society of Clinical Oncology Annual Meeting.

# Fruquintinib - FRESCO efficacy in 3L CRC

Third-Line Metastatic Colorectal cancer	Fruquintinib		Regorafenib		Regorafenib		Regorafenib		
	FRESCO		CONCUR		CONCUR		CORRECT		
	Mainland China		Chinese Patients (Mainland China, Hong Kong, Taiwan) [1]		Mainland China, Hong Kong, Taiwan, Vietnam, South Korea		Global		
Treatment arms	Fruquintinib	Placebo	Regorafenib	Placebo	Regorafenib	Placebo	Regorafenib	Placebo	
Patients (n)	278	138	112	60	136	68	505	255	
Complete Response, n (%)	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	
Partial Response, n (%)	4.3%	0.0%	3.6%	0.0%	4.4%	0.0%	1.0%	0.4%	
Stable Disease, n (%)	57.6%	12.3%	40.2%	6.7%	45.6%	7.4%	42.8%	14.5%	
Disease Control Rate, n (%)	62.2%	+49.9	45.5%	+38.8	51.5%	+44.1	41.0%	+26.1	14.9%
Median Progression-Free Survival (mPFS) (mo.)	3.7	+1.9	1.8	2.0	+0.3	1.7	3.2	+1.5	1.7
mPFS p-value	<0.001		not published		<0.0001		<0.000001		
mPFS Hazard Ratio	0.26		0.32		0.31		0.49		
Median Overall Survival (mOS) (mo.)	9.3	+2.7	6.6	8.4	+2.2	6.2	8.8	+2.5	6.3
mOS p-value	<0.001		not published		0.0002		0.0052		
mOS Hazard Ratio	0.65		0.56		0.55		0.77		

- **Good fruquintinib efficacy over regorafenib in Chinese patients** - specifically in terms of Disease Control Rate; median Progression-Free Survival and median Overall Survival.
- **FRESCO is a fully-powered Phase III registration study (n=416)** whereas **CONCUR was an under-powered Asia region study (n=204, including only 129 mainland Chinese patients [2])**.
- **CONCUR results should be regarded as directional only - China approval resulted from CORRECT study (n=760)**.

[1] Efficacy & safety of regorafenib monotherapy in Chinese patients with previously treated metastatic colorectal cancer: subgroup analysis of the CONCUR trial; R Xu; [2] China FDA website.

# Fruquintinib - FRESCO safety in 3L CRC

## High VEGFR selectivity - lower off-target AEs & more tolerable



Third-Line Metastatic Colorectal cancer ≥G3 AEs in >4% of Patients	Fruquintinib FRESCO		Regorafenib CONCUR	
	Mainland China TEAEs		Chinese Patients (Mainland China, Hong Kong, Taiwan) All AEs [1]	
Treatment arms	Fruquintinib	Placebo	Regorafenib	Placebo
Patients (n)	278	138	112	60
≥G3 AE (Safety population)	61.1%	19.7%	69.6%	46.7%
SAE (Safety population)	15.5%	5.8%	31.3%	26.7%
<b>VEGFR on-target related AEs:</b>				
Hypertension, ≥G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%
<b>Off-target (i.e. non-VEGFR) related AEs:</b>				
Hypophosphatemia, ≥G3	0.0%	0.0%	8.0%	0.0%
Hypokalemia, ≥G3	0.7%	0.7%	6.3%	0.0%
Rash/desquamation, ≥G3	0.0%	0.0%	4.4%	0.0%
Lipase increase, ≥G3	0.0%	0.0%	6.3%	1.7%
<b>Hepatic function (Liver function) AEs:</b>				
ALT increased, ≥G3	0.7%	1.5%	7.1%	3.3%
AST increased, ≥G3	0.4%	0.7%	8.9%	0.0%
Blood bilirubin increased, ≥G3	1.4%	1.5%	8.9%	8.3%
NOTE: Baseline Characteristics -- Liver metastasis	66.5%	73.9%	na	na
<b>Tolerability:</b>				
AE Leading to dose interruption	35.3%	10.2%	68.8%	25.0%
AE Leading to dose reduction	24.1%	4.4%	23.2%	0.0%
AE Leading to treatment discontinuation	15.1%	5.8%	14.3%	6.7%

### Fruquintinib far more selective than regorafenib

BIOCHEMICAL ACTIVITY	Fruquintinib IC <sub>50</sub> (nmol/L)	Regorafenib IC <sub>50</sub> (nmol/L)
<b>On-Target Kinases:</b>		
VEGFR1	33	13
VEGFR2	35	4.2
VEGFR3	0.5	46
<b>Off-Target Kinases:</b>		
Ret	128	1.5
FGFR1	181	202
c-kit	458	7
PDGFRβ	>10,000	22
RAF-1	>10,000	2.5
B-RAF	>10,000	28
B-RAF <sup>V600E</sup>	>10,000	19

### Regorafenib liver toxicity black-box warning:

- ➔ Increased liver function test monitoring (weekly if elevated) & remedial dose interruption.
- ➔ 3L CRC China - 65-75% liver metastasis - weaker pts.

STIVARGA (regorafenib) tablets, oral  
Initial U.S. Approval: 2012

#### WARNING: HEPATOTOXICITY

See full prescribing information for complete boxed warning. Severe and sometimes fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function prior to and during treatment. **Interrupt and then reduce or discontinue Stivarga** for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence. (2.2, 5.1)

# Fruquintinib - FALUCA Phase III in 3L NSCLC



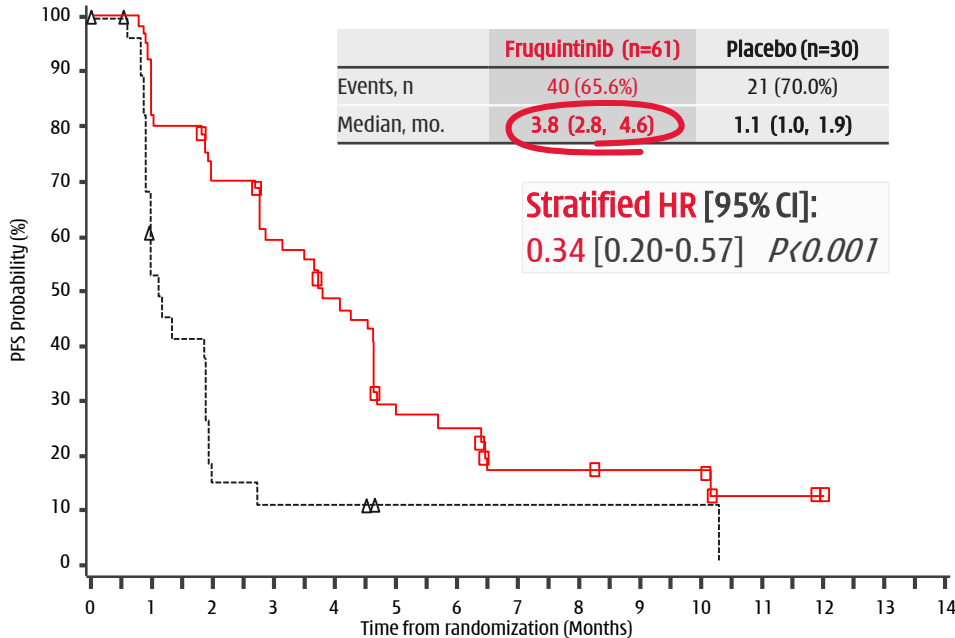
Phase III enrolment complete (n=527); top-line results Q4 2018

## Non-small cell lung cancer ("NSCLC") Phase II PoC Results

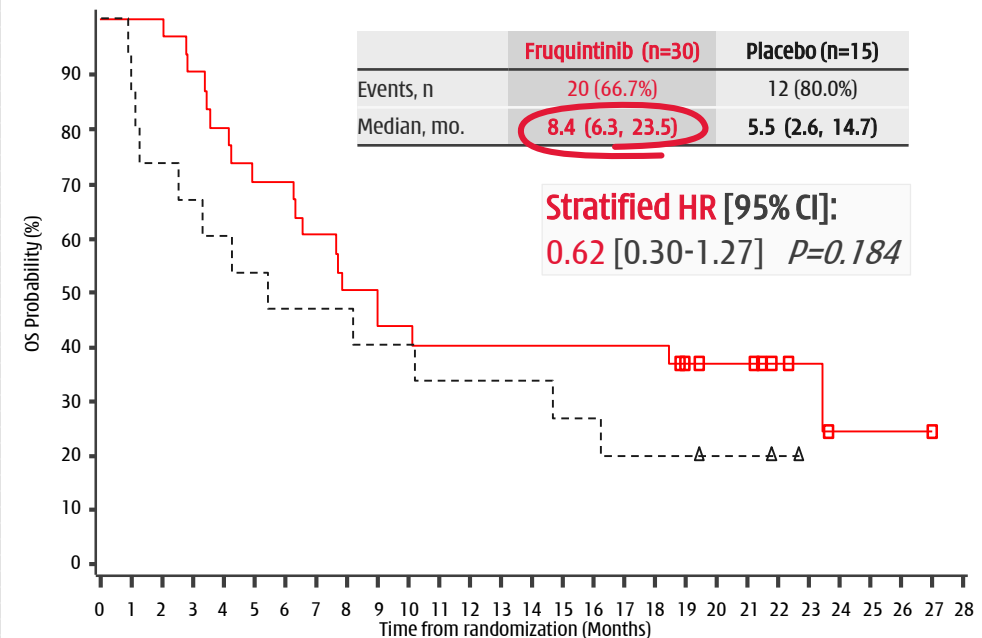
- ✓ 91 3L only patients **enrolled in ~9 months** (Jun'14-Mar'15).
- ✓ **Clearly met primary PoC endpoint** of reduction in risk of progression.
- ✓ **AEs consistent** with the known safety profile and generally superior versus ≥3L colorectal cancer Phase III with lower >Gr.3 AEs (32.8% vs. 61.1%) and dose reductions (13.1% vs. 24.1%).
- ✓ **Phase III FALUCA study enrolment completed in February 2018.**

Patients, %	Fruquintinib (n=61)	Placebo (n=30)
All AEs, any grade	61 (100%)	27 (90.0%)
All AEs, grade ≥3	20 (32.8%)	6 (20.0%)
Hypertension, grade ≥3	5 (8.2%)	1 (3.3%)
Hand-foot syndrome ("HFS"), grade ≥3	3 (4.9%)	0
All other AEs, grade ≥3 (each)	≤2 (≤3.3%)	0
Leading to dose interruption	9 (14.8%)	0
Leading to dose reduction	8 (13.1%)	0
Leading to treatment discontinuation	6 (9.8%)	1 (3.3%)

## 3L NSCLC Phase II: Progression-Free Survival



## 3L NSCLC Phase II: Overall Survival [1]



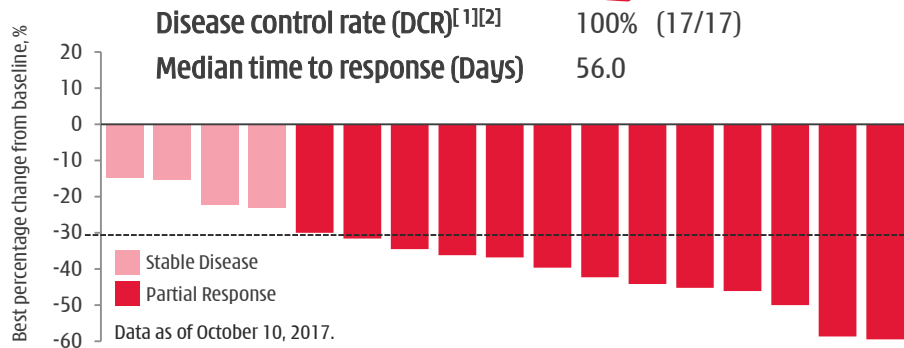
[1] EGFR Mutation positive (n=45)

# Fruquintinib - 1L NSCLC combo w/



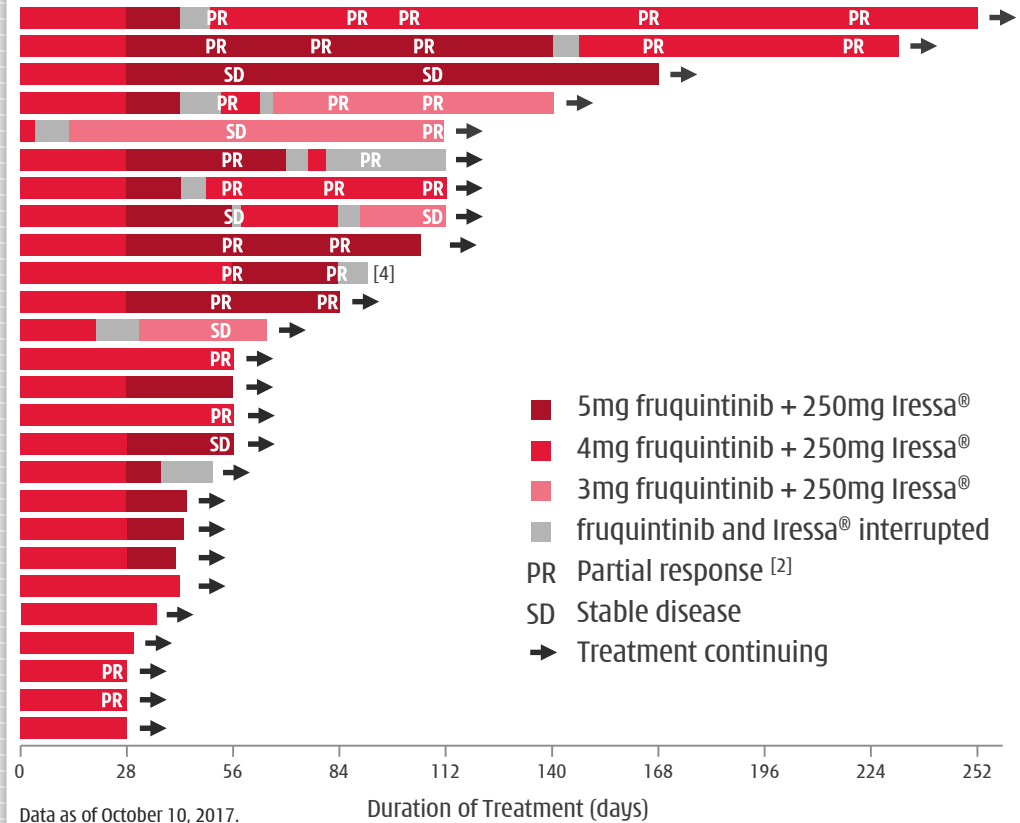
Two small molecule TKIs allow for better management of tox.

## 1. Promising efficacy in first line - 76% ORR (13/17). [1,2,3]



Disease control rate (DCR)<sup>[1][2]</sup> 100% (17/17)  
Median time to response (Days) 56.0

## 3. Combination of highly selective TKIs vs. mAbs: daily dose flexibility improves tolerability. This enables maintained drug exposure, leading to more durable response. [2,3]



## 2. Prelim. safety data: fruquintinib vs. other VEGFRis.

Adverse Events ("AEs")	Iressa® or Tarceva® FLAURA [5] N = 277, n (%)	Avastin® + Tarceva® [6] N = 75, n (%)	Fruquintinib + Iressa® N = 26, n (%) [3]
All AEs, any grade	273 (98%)	≥74 (≥99%)	23 (89%)
All AEs, Grade ≥3	124 (45%)	68 (91%)	8 (31%)
AEs leading to death	6 (2%)	0 (0%)	0 (0%)
AEs leading to VEGFRi discontin.	NA	31 (41%)	1 (4%)
<b>Grade ≥3 AEs:</b>			
Liver function (e.g. ALT, AST incr.)	33 (12%)	6 (8%)	6 (23%)
Hypertension	NA	45 (60%)	1 (4%)
Proteinuria	NA	6 (8%)	1 (4%)
Rash	13 (5%)	19 (25%)	0 (0%)
Decreased appetite	22 (8%)	1 (1%)	NA

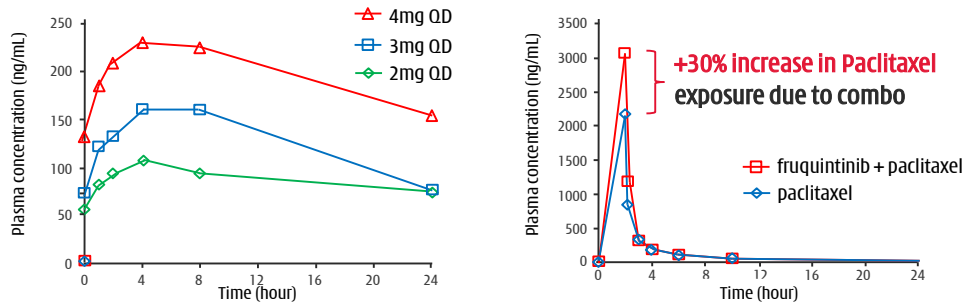
[1] Best tumor response for efficacy evaluable patients (patients who had both baseline and post-baseline tumor assessments); ORR = objective response rate; [2] Four PRs not yet confirmed at the time of data cut-off date; mAb = Monoclonal Antibody; [3] Lu, S., et al, "A Phase II study of fruquintinib in combination with gefitinib in stage IIIB/IV NSCLC patients harboring EGFR activating mutations", ID 10907 IASLC 18<sup>th</sup> World Conference on Lung Cancer, Yokohama, Japan, October 15-18, 2017; [4] Drug discontinuation due to Grade 3 proteinuria and Grade 3 QTc prolonged; [5] Ramalingam S. et al, "LBA2 PR Osimertinib vs standard of care (SoC) EGFR-TKI as first-line therapy in patients (pts) with EGFRm advanced NSCLC: FLAURA", ESMO 2017 Congress, Madrid, Spain, September 9, 2017; [6] Seto, T., et al, "erlotinib alone or with bevacizumab as first-line therapy in patients with advanced non-squamous non-small-cell lung cancer harbouring EGFR mutations (J025567): an open-label, randomised, multicenter, phase 2 study", The Lancet 2014, 15 (11) 1236-1244.

# Fruquintinib - Gastric combo with paclitaxel

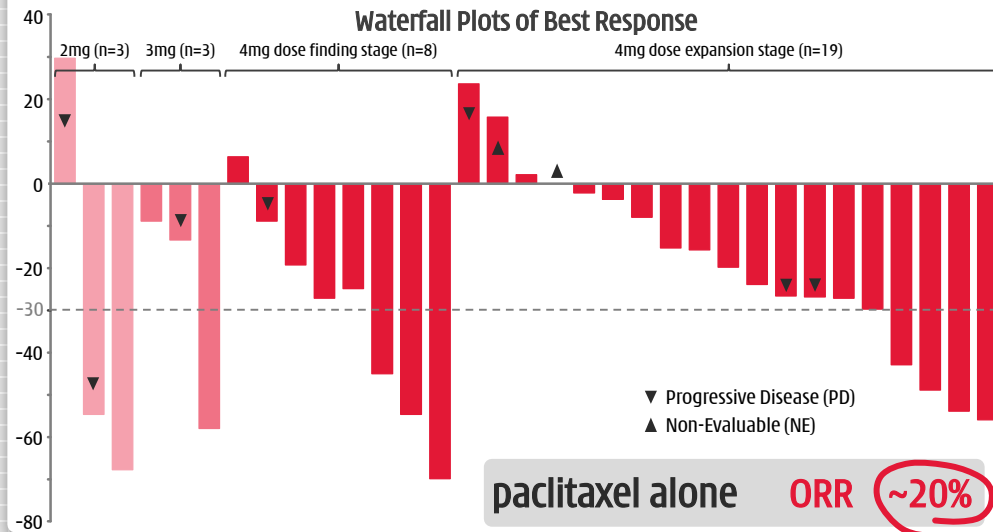


Phase III initiated Oct 2017 - Interim analysis planned mid-2019

1. **Dose proportional increase of fruquintinib AUC at steady state.** Over **30%** increase in paclitaxel drug exposure (mean  $AUC_{0-8}$ ) following multiple dose fruquintinib.



2. **ORR of 36%** (10/28) & **DCR of 68%** in efficacy evaluable pts. Fruquintinib 4mg,  $\geq 16$  wk. PFS of 50% &  $\geq 7$  mo. OS of 50%.



3. Encouragingly low level of dose reduction/interruption. Actual mean administered dose in the first cycle was **3.32mg/day for fruquintinib** (83.0% planned dose) & **78.6 mg/m<sup>2</sup>/week for paclitaxel** (98.3% planned dose).

Characteristics (Unit)	Drug Expansion Stage (N=19)	
	Fruquintinib 4 mg + paclitaxel 80 mg/m <sup>2</sup>	
	Drug interruption	Drug reduction
Dose modification with Fruquintinib N (%)	2 (10.5%)	2 (10.5%)
Dose modification with Paclitaxel N (%)	5 (26.3%)	1 (5.3%)

4. **AE profile in-line with expectations.** Neutropenia - a paclitaxel driven AE - with 57.9% Grade  $\geq 3$  AEs. **Similar to 60% level seen in RAINBOW study of ramcirumab (VEGF mAb) combo with paclitaxel in second-line gastric cancer.**

Drug related grade 3 or 4 AEs (NCI-CTCAE v 4.0) term	Dose Expansion Stage (N=19)
	Fruquintinib 4 mg + paclitaxel 80 mg/m <sup>2</sup>
Neutropenia	11 (57.9%)
Leukopenia	4 (21.0%)
Hypertension	2 (10.6%)
PLT decreased	1 (5.3%)
Anemia	1 (5.3%)
HFSR	1 (5.3%)
Mucositis oral	1 (5.3%)
Hepatic disorder	1 (5.3%)
Upper gastrointestinal hemorrhage	1 (5.3%)



# Other VEGFR TKI + PD-1 combinations in development



## PHASE III REGISTRATION STAGE COMBINATIONS

**1**

**1,800**

Lenvatinib  
+  
Pembrolizumab/  
Nivolumab

1L ccRCC,  
2L Endometrial Ca

US FDA BTD  
Jan-2018  
(Len+Pem)

NSCLC, RCC, Endometrial Ca, UC,  
HNSCC, Melanoma, HCC

**2**

**1,870**

Axitinib  
+  
Pembrolizumab/  
Avelumab

1L ccRCC,  
1L ccRCC\*,  
1L HCC, 2/3L NSCLC, 1L mUC

US FDA BTD  
Jul-2017  
(Axi+Pem)

US FDA BTD  
Dec-2017  
(Axi+Ave)

**3**

**1,440**

Cabozantinib  
+  
Nivolumab/  
Atezolizumab

1L ccRCC

UC, Genitourinary Ca, TNBC, RCC,  
NSCLC, CRPC, Ovarian Ca, Endometrial  
Ca, HCC, GC/GEJ, CRC, HNSCC, DTC

## EARLY EXPLORATORY STAGE COMBINATIONS

**1**

**716**

Apatinib  
+  
SHR-1210

1L HCC, 1L CCA, 2L HCC,  
2L NSCLC, 2L ED-SCLC,  
HCC, GC/GEJ, Sarcoma,  
solid tumors<sup>#</sup>

**2**

**300**

Regorafenib  
+  
Pembro/ Nivo /  
Avelumab

1L HCC, GC, MSS CRC,  
GIST, ESC, BTC, HCC

**3**

**50**

Sorafenib  
+  
PDR001

HCC

**4**

**32**

Tivozanib  
+  
Nivolumab

RCC

**5**

**18**

Nintedanib  
+  
Pembrolizumab

Solid tumors

**102<sup>\$</sup>**

Sunitinib / Pazopanib /  
Cediranib  
+  
Nivo / Pembr / Durva

RCC, Gynecologic Ca

Note: Numbers represent the total planned enrollment patients in clinical trials sponsored by industry players, including the numbers in control arms; 1 means Ph3 registration trials; 2 means early exploratory trials; 3 means failed trials;

Source: CT.gov, data correct as of June 10, 2018; \* two Ph3 registration trials in 1L ccRCC, that is NCT02853331 and NCT02684006; # including an triplet combination of VEGFR TKI + αPD-1 + IDO1, that is NCT03491631 (Apatinib/SHR-1210/SHR-9146); \$ data from ASCO 2014 #5010, ASCO 2014

57 #5010, ASCO 2017 #4506 and J Clin Oncol 2017 35(19) 2193-202.



# Sulfatinib

*A highly active TKI with a unique angio-immuno Mechanism of Action*

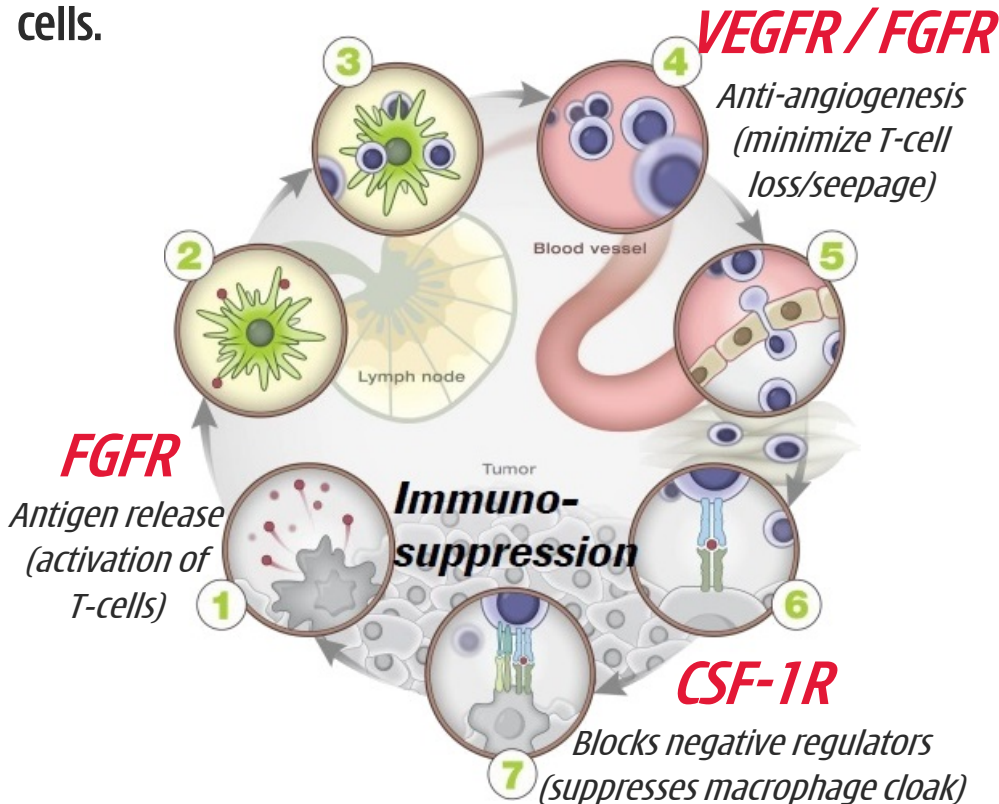


# Sulfatinib's unique angio-immuno kinase profile



Multi-indication global development program, initially for NETs<sup>[1]</sup>

Sulfatinib's unique **angio-immuno kinase profile & MoA<sup>[1]</sup>** activates & enhances the body's immune system, namely T-cells, via VEGFR/FGFR while inhibiting the production of macrophages (CSF-1R) which cloak cancer cells.



**Activity 1: Aiming for fast/first approval in China for all NET<sup>[2]</sup> patients - 2x pivotal Phase III trials in**

Progress	Pancreatic NET Phase III	Non-Pancreatic NET Phase III
Primary site	Pancreas	GI, lung, other or unknown
Population	Unresectable or metastatic disease; well differentiated (G1/G2); ≤2 prior systemic drugs.	
# of Sites	20-30 (China)	
# of Patients	~195	~270
Study design	Double-blind. Randomized 2:1 to sulfatinib or placebo, until PD. Predefined interim analysis.	
Dosage	Sulfatinib 300mg QD, 28 days per cycle (vs. placebo)	
Primary Endpoint	Progression-Free Survival (PFS) by BICR evaluation	
Secondary Endpoints	Overall Survival (OS), ORR, safety, etc.	
First Patient In / Readout	March 2016 / 2019	December 2015 / 2019

**Activity 2: Global development**

- U.S. Phase I (dose escalation) in solid tumors completed
- U.S. Phase Ib/II initiated in July 2018, focusing on pancreatic NET and biliary tract cancer.

**Activity 3: Exploratory PoC<sup>[3]</sup> in other indications**

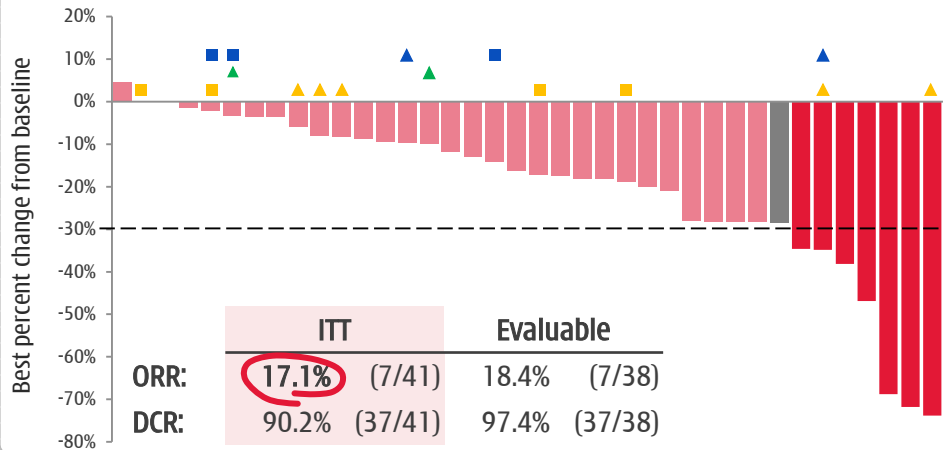
- China Ph.II studies underway in: (a) medullary thyroid cancer; (b) differentiated thyroid cancer; and (c) biliary tract cancer.

# Sulfatinib - China NET - Phase II (ENETS 2017<sup>[1]</sup>)

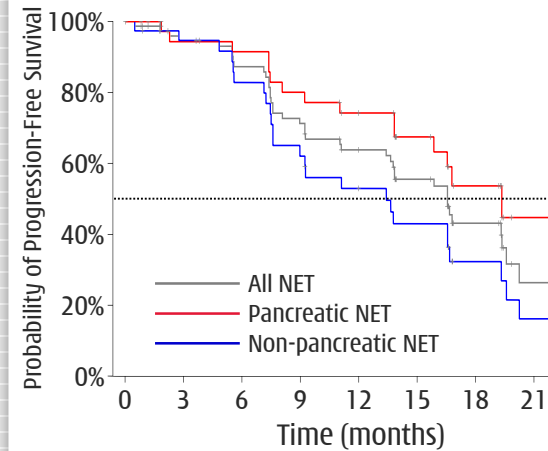
## Efficacy in all NET & patients who failed on Sutent®/Afinitor®



### Phase II: Pancreatic NET - Highest ORR seen to date in pNET.



### Phase II: Progression-Free Survival (PFS)

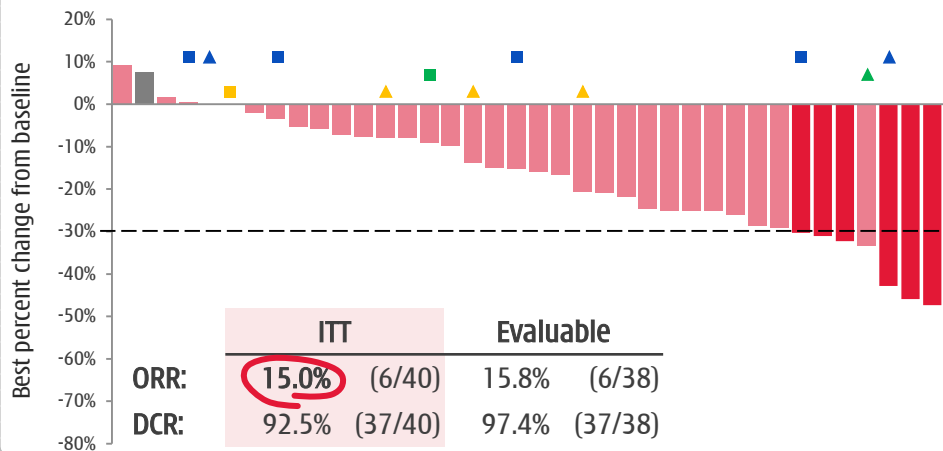


	Median PFS (months)	PDs or Deaths (% pts)
All NET (n=81)	16.6m (13.4, 19.4)	51.9% (42/81)
P-NET (n=41)	19.4m (13.8, 22.1)	39.0% (16/41)
Non-P NET (n=40)	13.4m (7.6, 16.7)	65.0% (26/40)

Data has yet to reach maturity - data cut-off as of Jan 20, 2017.

■ Partial Response  
 ■ Stable Disease  
 ■ Progressive disease  
 ■ Prior Sutent®  
 ■ Prior Faminitinib (VEGFR)  
 ■ Prior Afinitor®  
 ▲ Progressive Disease on Prior TKI

### Phase II: Non-Pancreatic NET - High ORR in non-pNET also.



### Phase II: Safety - Well tolerated - Adverse Events manageable.

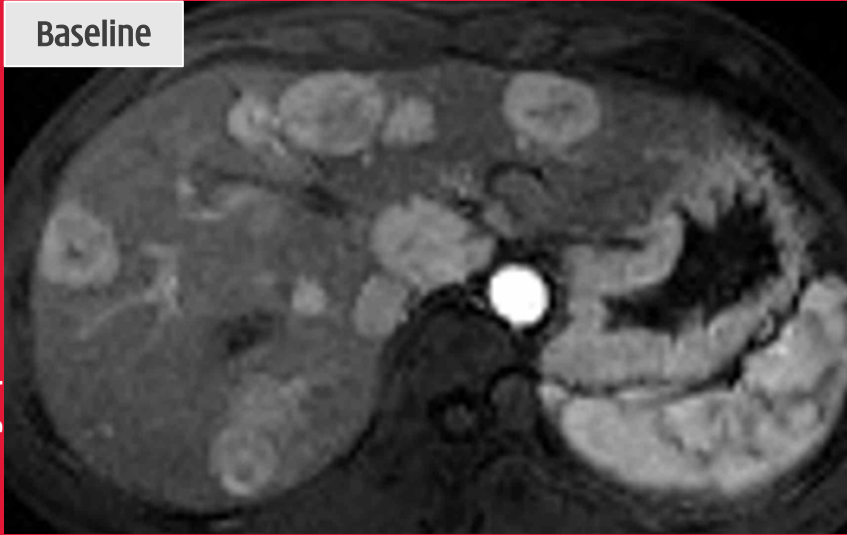
	Grade ≥3 (≥4pts) n (%)	Adverse Events ("AEs") - Regardless of causality	N=81 n (%)
Hypertension	25 (30.9)	Any AE	81 (100.0)
Proteinuria	11 (13.6)	Grade ≥3 AE	63 (77.8)
Hyperuricemia	8 (9.9)	Any SAE	21 (25.9)
Hypertriglyceridemia	7 (8.6)	Any drug-related AE	81 (100)
Diarrhea	6 (7.4)	Any drug-related grade ≥3 AE	58 (71.6)
ALT increased	5 (6.2)	Any drug related SAE	10 (12.3)
Anemia	4 (4.9)	<b>Drug related AE leading to:</b>	
Hypokalemia	4 (4.9)	<b>dose interruption</b>	40 (49.4)
Hepatic function abnormal	4 (4.9)	<b>dose reduction</b>	20 (24.7)
		<b>drug withdrawal</b>	7 (8.6)

# Sulfatinib - China NET - Phase II (*ENETS 2017*<sup>[1]</sup>)

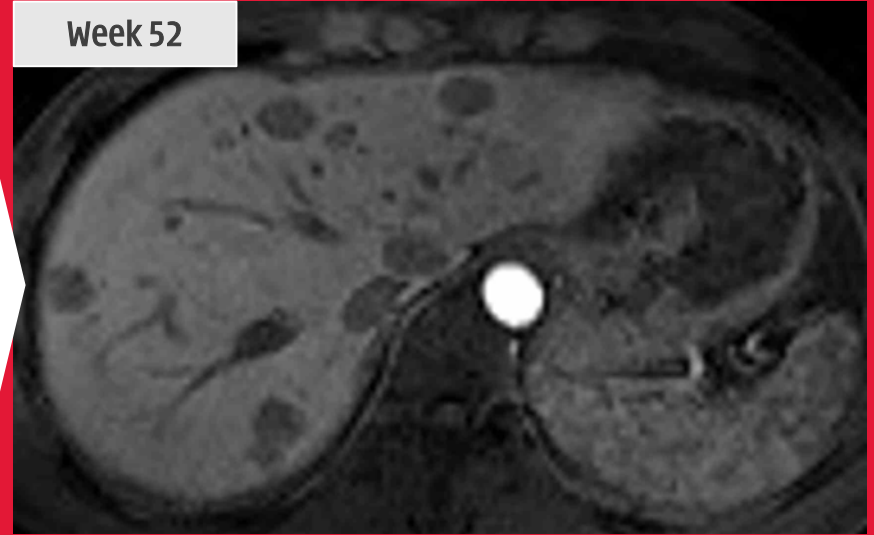
## Tumor devascularization & central necrosis

Patient 1  
Duodenum NET G2  
w/ multiple liver & retroperitoneal lymph node metastases

Baseline

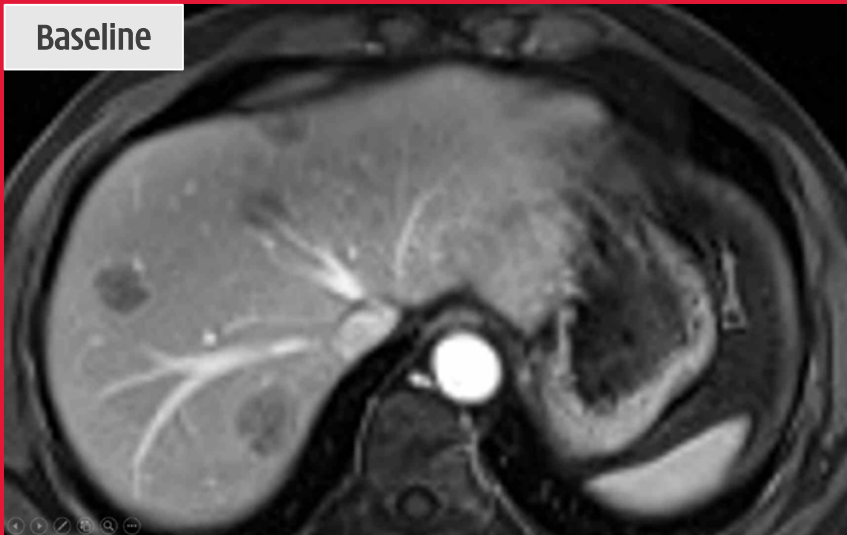


Week 52



Patient 2  
Rectum NET G2  
w/ multiple liver metastases

Baseline



Week 56





# Epitinib

*EGFR mutation kinase inhibitor that penetrates the blood-brain barrier*

*Entering Phase III trials*



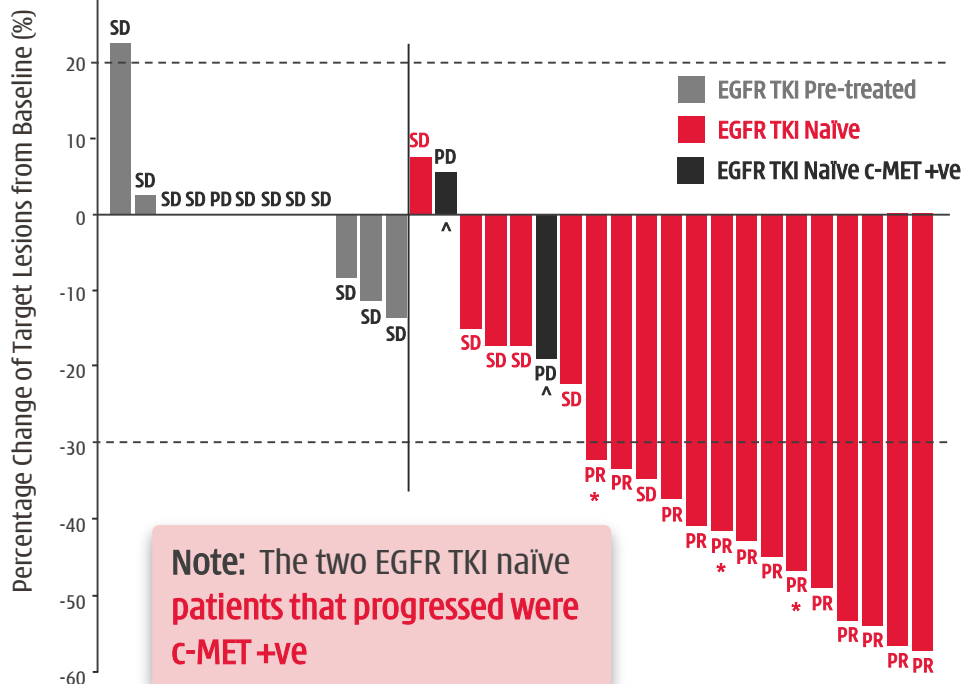
# Epitinib - 70% response in NSCLC w/ brain mets<sup>[1]</sup>



Unmet medical need for ~50% of NSCLC patients w/ brain mets<sup>[2]</sup>

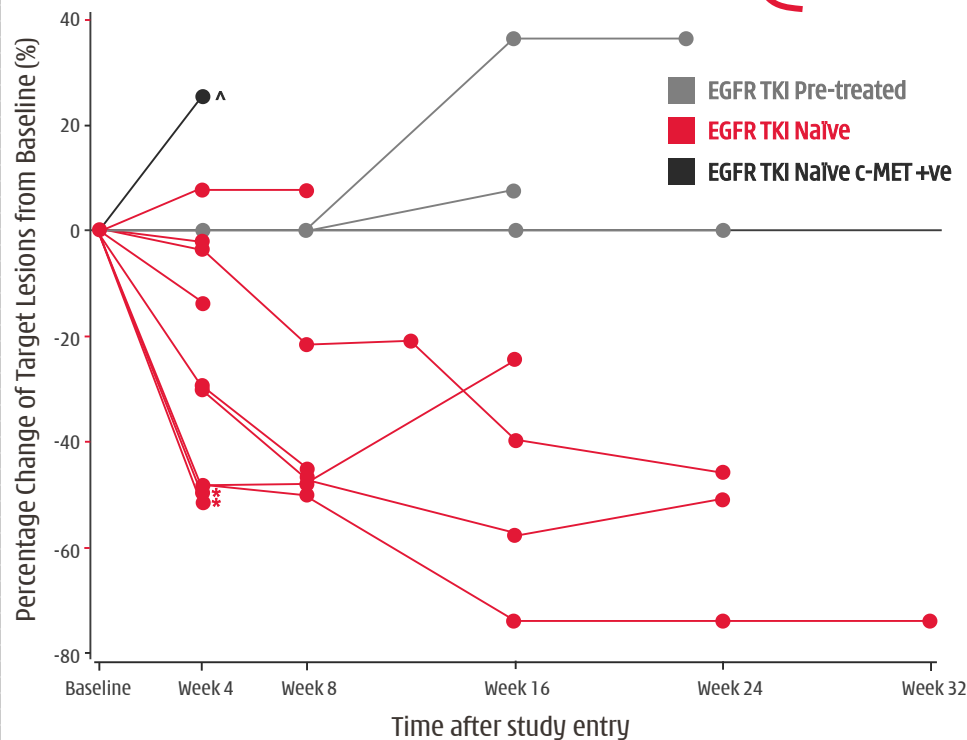
## 1. Phase Ib<sup>[1]</sup> - epitinib monotherapy in EGFRm+ NSCLC patients - efficacy in lung in-line with Iressa®/Tarceva®.

160mg once daily dose ("QD")	EGFR TKI naïve (N=21)	EGFR TKI naïve excl. c-MET +ve (N=19)
Objective Response Rate ("ORR")	61.9% (13/21) #	68.4% (13/19) #
Disease Control Rate ("DCR")	90.5% (19/21) #	100.0% (19/19) #



## 2. Phase Ib<sup>[1]</sup> - solid/durable efficacy in brain in EGFRm+ NSCLC patients with measurable brain mets (>10mm).

160mg QD dose	EGFR TKI naïve (N=11)	EGFR TKI naïve excl. c-MET +ve (N=10)
Intracranial ORR	63.6% (7/11) #	70.0% (7/10) #
Intracranial DCR	90.9% (10/11) #	100.0% (10/10) #

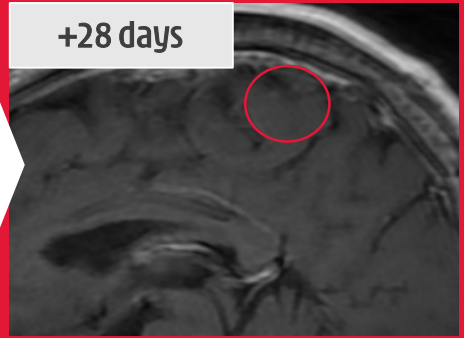
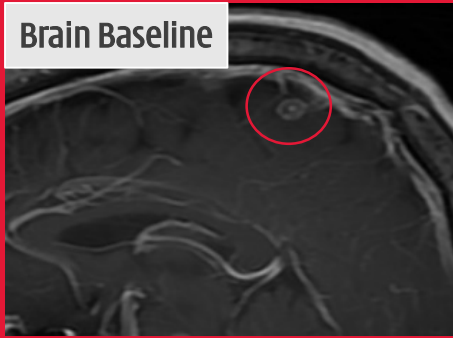
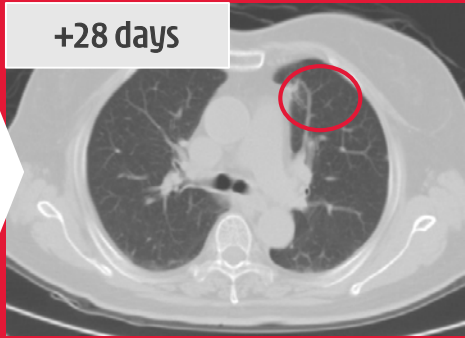
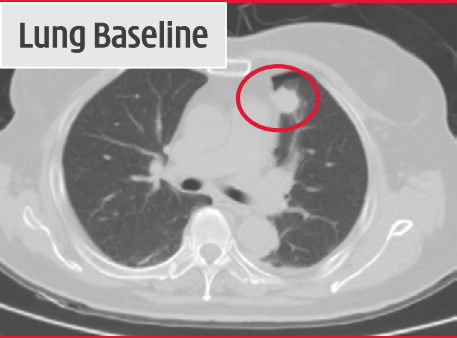


[1] Dose expansion stage - data cut-off September 20, 2016; [2] Li B, Bao YC, Chen B, *et al.* Therapy for non-small cell lung cancer patients with brain metastasis. Chinese-German J Clin Oncol, 2014, 13: 483-488;

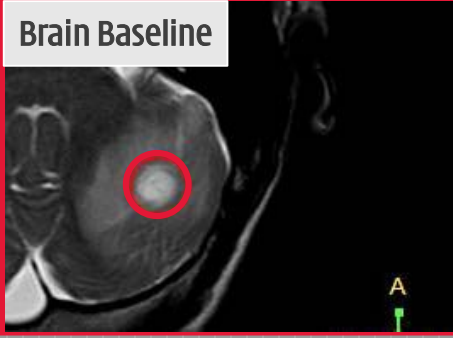
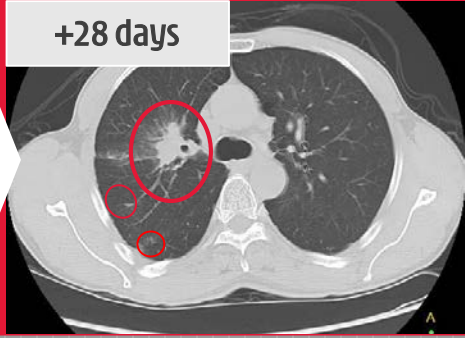
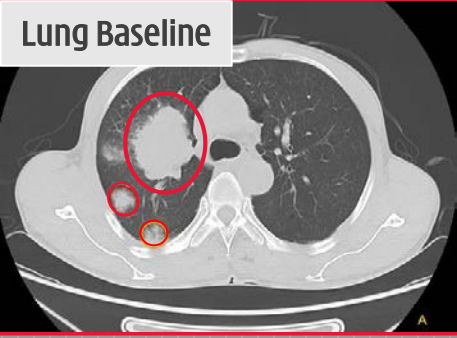
\* Unconfirmed PR, due to no further assessment at cut-off date; # Includes both confirmed and unconfirmed PRs; ^ c-MET amplification/high expression identified.

# Epitinib - Strong PoC efficacy - 160mg QD dose

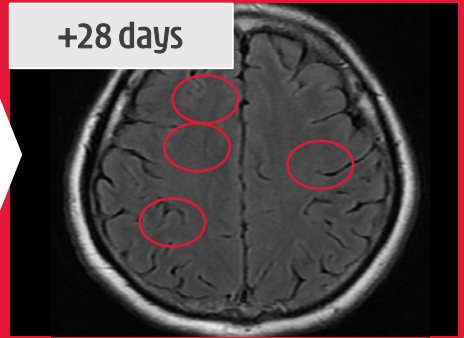
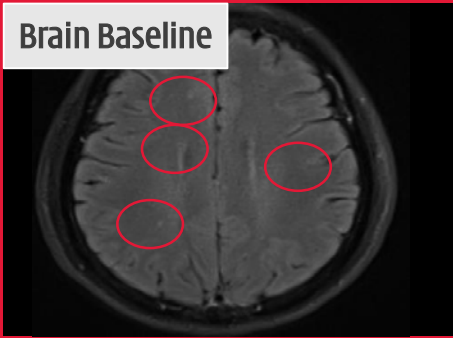
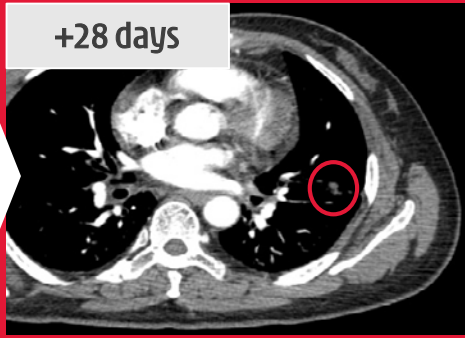
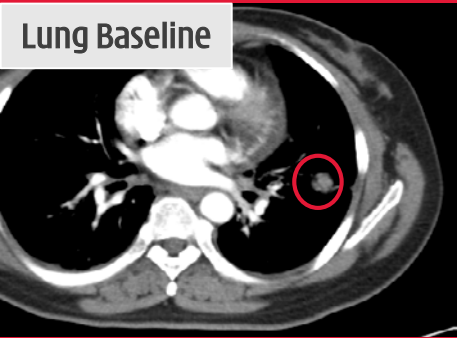
**62-year-old female**



**57-year-old male**



**52-year-old male**





# Epitinib - Safe & well tolerated

Pivotal Phase III study to initiate in late 2018

3. Epitinib **well tolerated** by patients<sup>[1]</sup> w/advanced solid tumors. Safety profile is consistent with that of approved EGFR-TKIs (e.g. Iressa®/ Tarceva®).

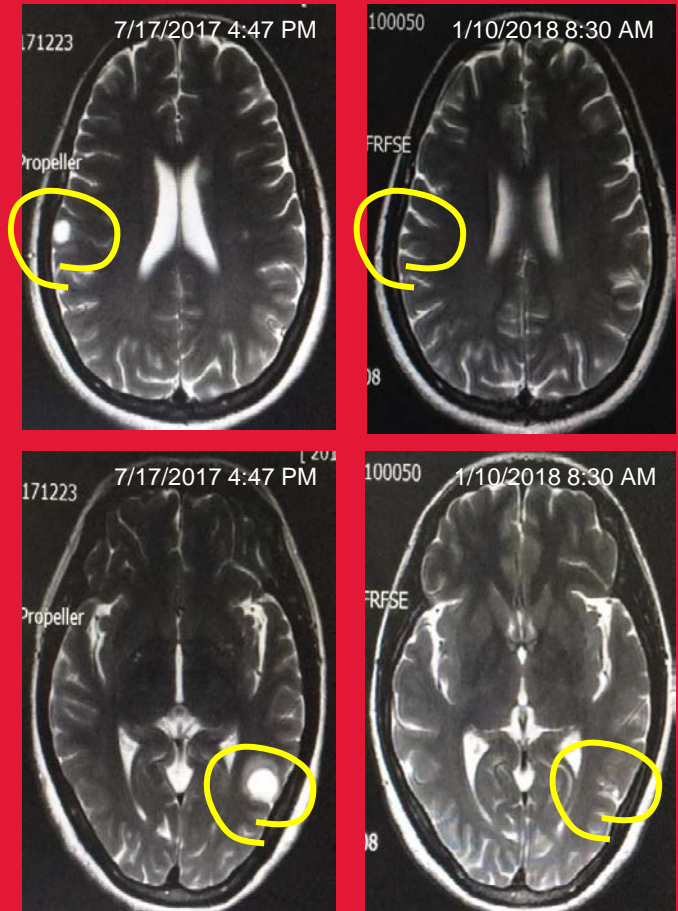
Dose Escalation Stage (n=35*) (Drug related AEs reported >10%)			Dose Expansion Stage (n=37) (Drug related AEs reported >10%)		
160mg QD dose	All Grades n (%)	Grade 3/4 n (%)	160mg QD dose	All Grades n (%)	Grade 3/4 n (%)
Skin rash	21 (60.0%)	1 (2.9%)	Skin rash	31 (83.8%)	2 (5.4%)
Diarrhea	12 (34.3%)	-	Hyper-pigmentation	18 (48.6%)	1 (2.7%)
AST increase	12 (34.3%)	1 (2.9%)	ALT increase	15 (40.5%)	7 (18.9%)
ALT increase	11 (31.4%)	1 (2.9%)	AST increase	15 (40.5%)	4 (10.8%)
Total bilirubin increase	10 (28.6%)	2 (5.7%)	ASP increase	11 (29.7%)	1 (2.7%)
Stomatitis	5 (14.3%)	-	Diarrhea	10 (27.0%)	-
Exfoliative dermatitis	5 (14.3%)	-	Proteinuria	10 (27.0%)	-
Pruritus	5 (14.3%)	-	Total bilirubin increase	9 (24.3%)	1 (2.7%)
Hyper-pigmentation	4 (11.4%)	-	Hyperuricemia	9 (24.3%)	2 (5.4%)
Gamma-GGT increase	4 (11.4%)	2 (5.7%)	Gamma-GGT increase	7 (18.9%)	4 (10.8%)
Conjugated bilirubin	4 (11.4%)	1 (2.9%)	Stomatitis	6 (16.2%)	-

4. Now **moving into Phase III** pivotal study in China.

- Phase III in 1L NSCLC with brain metastasis to start:
  - **Published positive Phase Ib expansion results** at WCLC 2016.
  - China FDA Phase III clinical trial cleared in July 2016.
  - **Finalized dose in early 2018 (120mg vs. 160mg QD), then initiating Phase III in late 2018.**
- EGFR gene amplified Glioblastoma (primary brain tumors):
  - **Phase Ib/II proof-of-concept underway.**

## CASE STUDY - EGFR-TKI naïve patient

- Male, 46, diagnosed with Stage IV **NSCLC adenocarcinoma** (Exon21)
- Metastases in the brain, meninges, & bone
- 1<sup>st</sup>-line chemo naïve
- 120mg QD dosage**
- 25 weeks (177 days) on treatment with clear response in multiple measurable (>10mm diameter) brain lesions



[1] No Dose Limiting Toxicity ("DLT") was observed in any cohort; \* One patient did not join multiple dosing.

A composite background image. The top left shows a close-up of a person in a white lab coat using a pipette to transfer liquid into a multi-well plate. The top right shows a person's hand pointing at a whiteboard with blue chemical structures drawn on it. The bottom of the slide features a white text box with red text.

## Additional Clinical Candidates

*HMPL-523, Theliatinib, HMPL-689, HMPL-453 & HM0046599...*

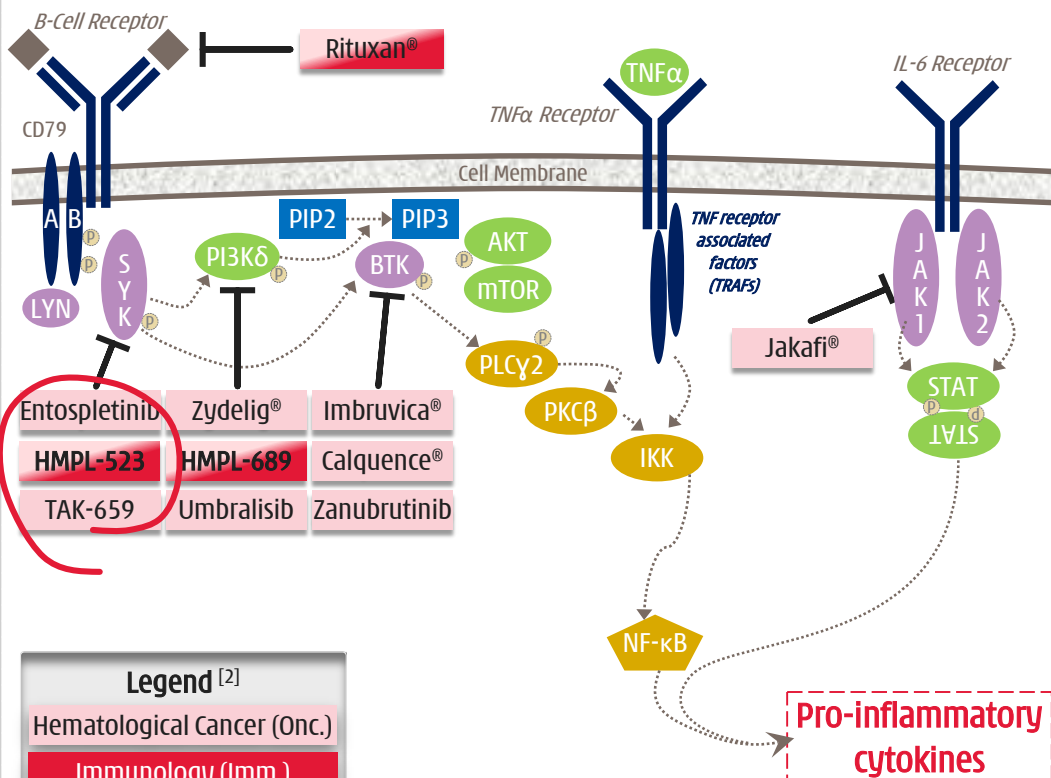
*...all progressing as planned*

# HMPL-523 - hematological malignancies

## Syk exciting target emerging - Lymphoma PoC ongoing

1. The B-cell signaling is **critical in hematological cancer** with three **breakthrough therapies** recently approved.

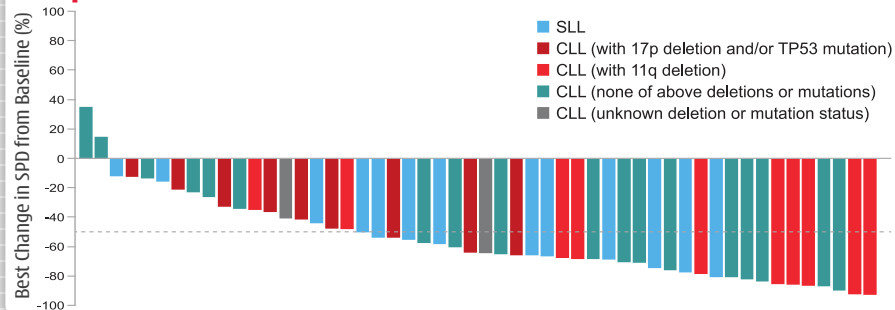
- 2017 sales: Imbruvica® \$1.9bn; Zydelig® \$0.5bn; Jakafi® \$1.1bn; & Rituxan® \$6.0bn [1].



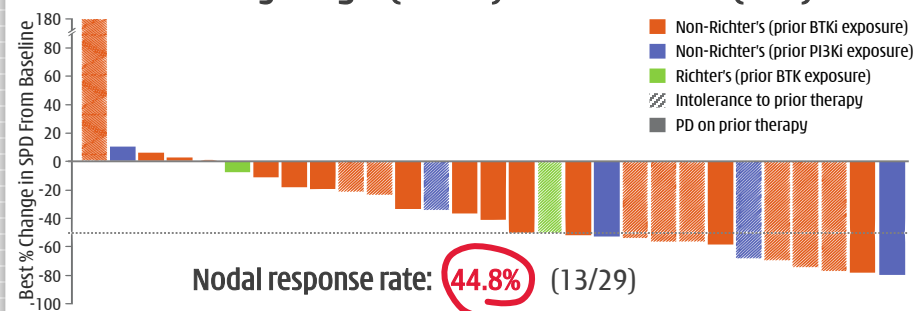
**Legend [2]**

Hematological Cancer (Onc.)
Immunology (Imm.)

2. Entospletinib ASH [3] Dec 2015 data - **65% Nodal Response Rate** in CLL & SLL [4] [5].



3. Entospletinib potential for **overcoming resistance/intolerance** to Zydelig® (PI3Kδ) & Imbruvica® (BTK) [5].



4. Entospletinib **not a perfect compound** [6].

- Poor solubility/oral absorption & high variation in drug exposure.
- Some CYP [6] inhibition & increased risk of drug-drug interaction.
- 66% Grade ≥3 AEs, **49% SAEs**, **46% drug interruption** & 20% disco.

[1] Rituxan® 2017 sales in oncology only; [2] Approved Drug = ®; All others are clinical candidates; [3] ASH = American Society of Hematology; [4] Chronic Lymphocytic Leukemia ("CLL") & small lymphocytic lymphoma ("SLL"); [5] Sharman et al, ASH Meetings 2015 & 2016; [6] CYP3A4, CYP2D6 and CYP 1A2.

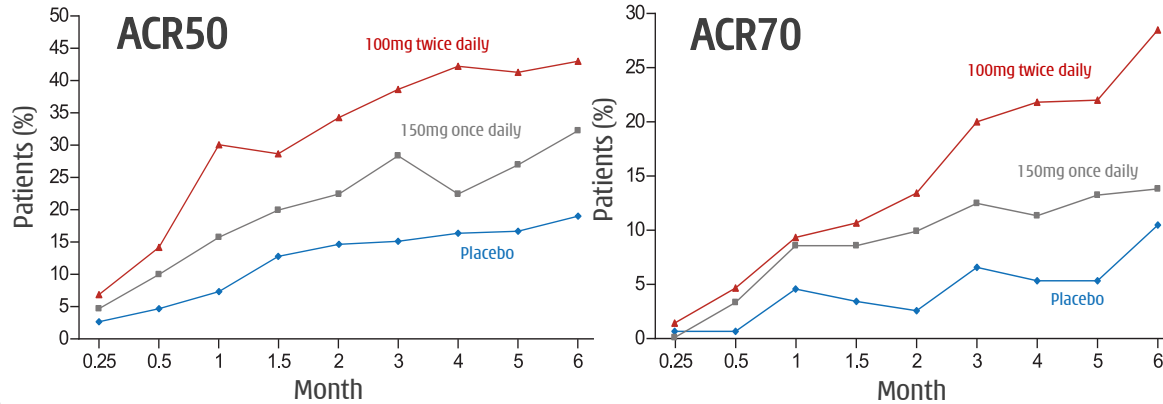
# HMPL-523 - immunology potential

Superior selectivity, better target coverage & efficacy vs. fosta.



## 1. Fostamatinib good Phase II<sup>[1]</sup> RA<sup>[2]</sup> dose response...

...but GI toxicity, infection & 23% put on antihypertensives.



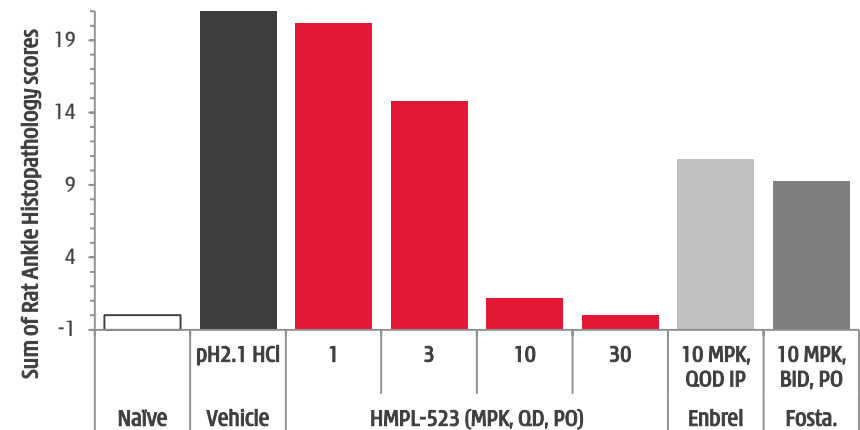
Percent of patients	Placebo (n = 153)	150mg QD (n = 152)	100mg BID (n = 152)
Diarrhea	3.0%	11.8% †	19.1% †
Upper respiratory infection	7.1	7.2	14.5 †
Urinary tract infection	4.6	3.3	5.9
Nausea	4.6	5.9	4.6
Neutropenia	0.7	6.6 †	5.9 †
Headache	5.2	6.6	5.9
Abdominal pain	2.6	6.6 †	5.9 †
ALT >3X ULN	2.0	3.9	3.9
Dizziness	2.0	2.6	4.6
Hypothyroidism	2.6	2.6	3.3
Cough	2.6	2.0	3.3

† P < 0.05 for comparison with placebo group; ALT = alanine aminotransferase.

## 2. HMPL-523 - far superior selectivity to fostamatinib...

...and very strong efficacy in preclinical RA models.

Selectivity	HMPL-523 IC <sub>50</sub> (nM)	fostamatinib IC <sub>50</sub> (nM)
Syk enzyme	25 ± 5 (n=10)*	54 ± 16 (n=10)*
JAK 1,2,3 enzyme	>300, >300, >300*	120, 30, 480*
FGFR 1,2,3	>3,000, >3,000, >3,000	89, 22, 32*
FLT3 enzyme	63*	9*
LYN enzyme	921*	160*
Ret enzyme	>3,000*	5**
KDR enzyme	390 ± 38 (n=3)*	61 ± 2 (n=3)*
KDR cell	5,501 ± 1,607 (n=3)*	422 ± 126 (n=3)*

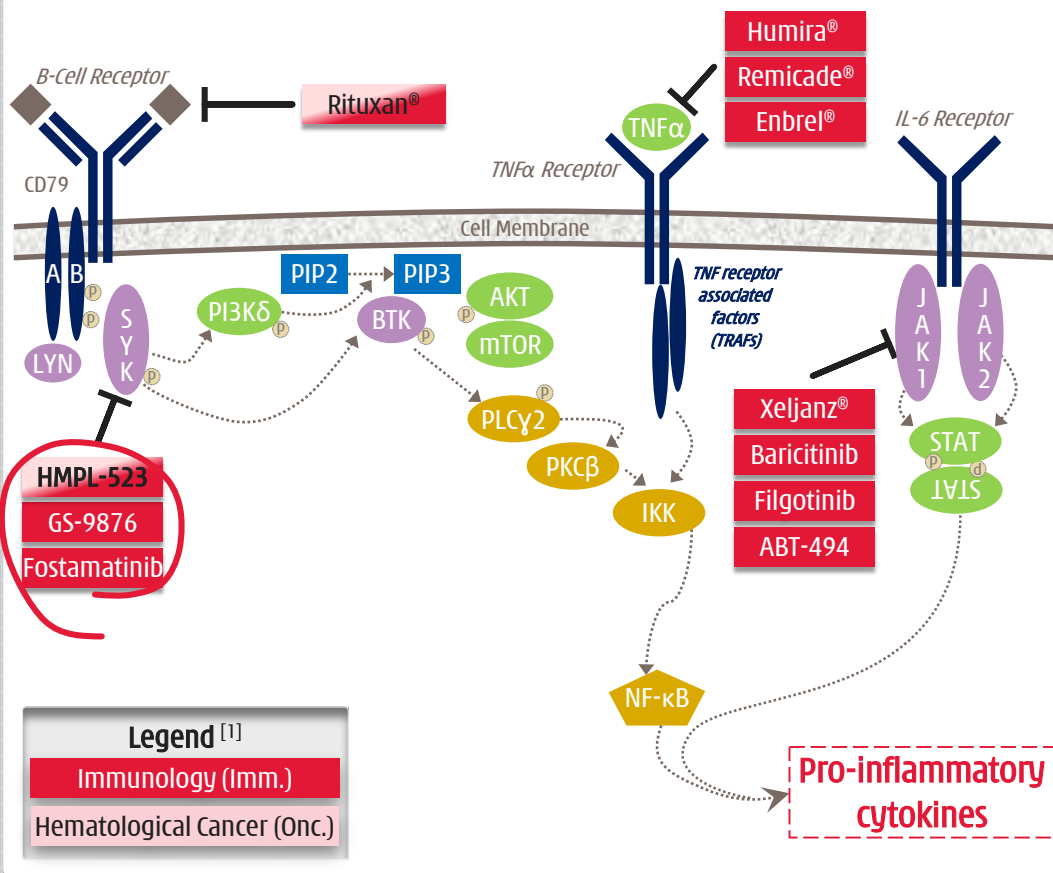


[1] Fostamatinib is a prodrug of the SYK inhibitor R406 - Phase II study data per N ENGL J MED 363;14; \*: HMPL data and Eun-ho Lee, 2011; \*\*: Birth Defects Research (Part A) 2009, 85: 130-6; [2] RA = Rheumatoid Arthritis; GI = Gastrointestinal; QD = one dose per day; BID = two doses per day; QOD = one dose every other day; PO = by mouth (i.e. orally); IP = by Intraperitoneal injection; Naive = model score without induced arthritis.

# HMPL-523 - immunology potential

## US Phase II in planning

1. Syk, the **most upstream B-cell pathway kinase target** is **clinically validated in rheumatoid arthritis ("RA")**, but we believe currently Chi-Med & Gilead are the only companies pursuing.



2. RA expected to be a **\$45 billion<sup>[2]</sup> market in 2020** with B-cell pathway; anti-TNF; & JAK the main focus.

(Methotrexate-IR: placebo adjusted)	ACR20	ACR50	ACR70	2017 Sales (\$ billion) <sup>[3]</sup>
<b>B-Cell receptor -- mAbs</b>				
Rituxan® (24-Week)	33%	21%	11%	1.6
<b>Anti-TNFα/NF-κB -- mAbs</b>				
Humira® (24-Week)	33%	29%	18%	18.4
Remicade® (24-Week)	30%	22%	8%	6.3
Enbrel® (24-Week)	44%	36%	15%	7.9
<b>JAK Inhibitors -- Small molecules</b>				
Xeljanz® (24-Week)	25%	23%	13%	1.3
Xeljanz® (12-Week)	28%	21%	8%	
baricitinib 4mg QD (12-Week)	30%	28%	14%	n/a
filgotinib 100mg BID (12-Week)	35%	40%	23%	n/a
ABT-494 24mg QD (12-Week)	32%	24%	18%	n/a
<b>Syk Inhibitor -- Small molecule</b>				
fostamatinib 100mg BID (24-Week)	32%	24%	18%	n/a

3. Substantial market potential remains in RA.

- mAbs intravenous administration and shut down immune system for 4-6 weeks - **high infection / lymphoma risks**.
- First-in-class JAKs in RA limited by **compound-related tox**.
- Syk inhibition shown to benefit patients - but **fostamatinib failed due to major off-target toxicity**.

[1] Approved drug = ®; All other clinical candidates: mAb = antibody (extracellular); small molecule (intracellular); [2] Frost & Sullivan; [3] 2017 sales in immunology only.

# Theletinib - encouraging activity observed

Potent & highly selective TKI - strong affinity to EGFRwt kinase



## 1. Major unmet medical need for wild-type EGFR activation tumors.

- EGFR activation affects multiple tumor types. Current EGFR TKIs are less effective in treating solid tumors with wild-type EGFR activation (gene amplification & protein over expression).
- Phase Ib expansion study on theletinib in esophageal cancer is currently underway in China.

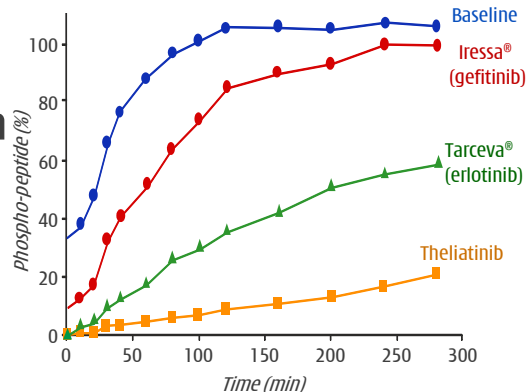
Tumor Types	Wild-type: Gene Amplification	Wild-type: Over Expression	Mutations
NSCLC	29%	62%	10-30%
Esophagus	8-30%	30-90%	12% (esophageal adenocarcinoma)
Stomach	29%	44-52%	<5%
Glioblastoma	36-51%	54-66%	27-54% (EGFR variant III)
Colorectal	4.5%	53%	8%
Head and neck	10-30%	66-84%	42% (EGFR variant III)

TKIs approved: Iressa®, Tarceva®

MABs approved: Erbitux®, Vectibix®

## 2. Superior anti-tumor activity of theletinib in pre-clinical studies with wild-type EGFR.

- 5-10-fold more potent than Tarceva®.
- Sustained target occupancy.



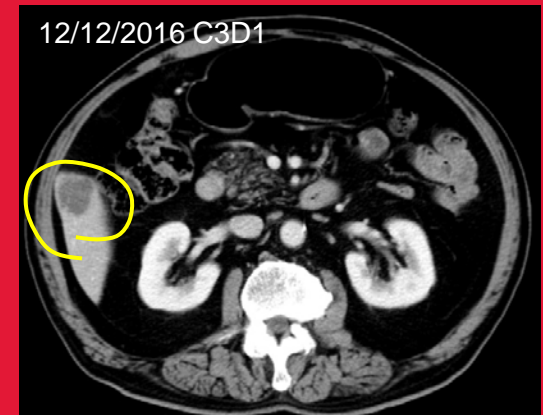
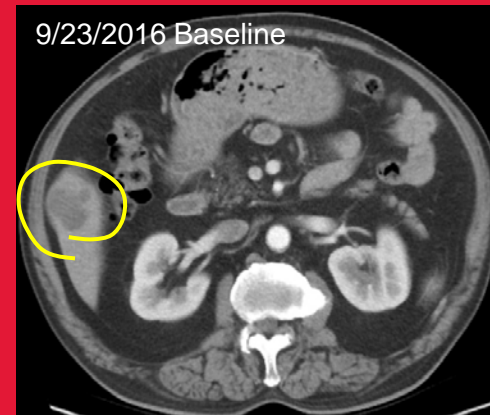
## 3. Esophageal cancer (EC): No effective treatment options.

- Major issue in Asia with poor prognosis: 5 year survival 10-20%

	new cases/year	deaths/year
U.S.	16,940 <sup>[1]</sup>	15,690 <sup>[1]</sup>
China	477,900 <sup>[1]</sup>	375,000 <sup>[1]</sup>

## CASE STUDY - EGFR protein over expression

- May 4, 2016: Man, 62, stage IV **esophageal squamous cell cancer** cT3N0M1 with **liver metastasis**. **High protein overexpression** - EGFR IHC local test: >75% of tumor cells 3+.
- May 4 to Sep 23, 2016: nimotuzumab/placebo + paclitaxel + cisplatin - **6 cycles with best tumor response: PD.**
- Oct 11, 2016: began theletinib 400mg daily.
- Dec 12, 2016: Cycle 3 Day 1 (C3D1) tumor assessment: **Target lesion (liver metastasis) shrank -33%** (36mm to 23mm diameter) - unconfirmed PR.
- Jan 23, 2017: Withdrew from study due to AEs - Gr 1 (diarrhea/pruritus/dental ulcer), Gr 2 (epifolliculitis/dermatitis).



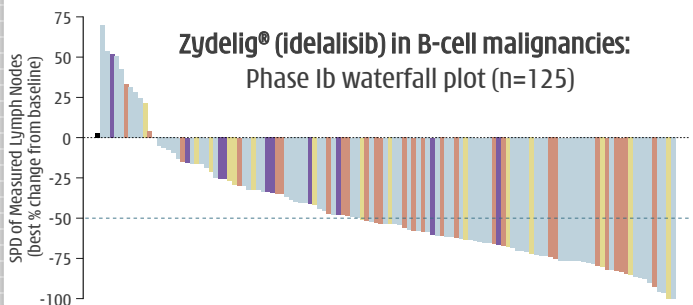
# HMPL-689 - Phase I Australia & China ongoing

## Designed to be a best-in-class inhibitor of PI3Kδ



### 1. PI3Kδ now a proven target.

- PI3Kδ activation associated with allergy, inflammation & oncology.
- Evidence that PI3Kδ inhibitors effective in ibrutinib-resistant mutant population.



### 2. PI3Kδ inhibitors being developed in a very broad range of indications.

Compound		Indication	Status	Issue
Zydelig® (idelalisib) PI3Kδ	Gilead	Chronic lymphocytic leukaemia, non-Hodgkin's lymphoma	Marketed	High incidence of liver toxicity seen with idelalisib (150mg bid)
AMG-319 PI3Kδ	Amgen	B-cell lymphoma, non-Hodgkin's lymphoma, T-cell lymphoma, chronic lymphocytic leukaemia	Phase I Trial	
Copiktra® (duvelisib) PI3Kγ/δ	Verastem/ Infinity [1]	Relapsed or refractory chronic lymphocytic leukaemia / small lymphocytic lymphoma	Approved	Need to spare PI3Kγ -- serious infection seen & associated with a boxed warning for 4 fatal and/or serious toxicities
		Relapsed or refractory follicular lymphoma	Approved [2]	
		Peripheral T-cell lymphoma	Phase II enrolling	
Aliqopa® (copanlisib) PI3Kα/δ	Bayer	Relapsed follicular B-cell non-Hodgkin lymphoma	Approved [2]	Serious and fatal infections and AEs

### 3. HMPL-689 -- Important asset.

Designed to improve on existing PI3Kδ inhibitors:

- Improved isoform selectivity (sparing PI3Kγ).
- Improved potency at whole blood level (>5X more potent than idelalisib) to cut compound related toxicity.
- Improved PK properties particularly efflux and drug/drug interaction due to CYP inhibition / induction, critical for combo therapy.

### 4. More potent / more selective than Zydelig®, Copiktra® & Aliqopa®.

Enzyme IC <sub>50</sub> (nM)	HMPL-689	Zydelig®	Copiktra®	Aliqopa®
PI3Kδ	0.8 (n = 3)	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 (142X)	104 (52X)	2 (2X)	6.4 (9X)
PI3Kα (fold vs. PI3Kδ)	>1,000 (>1,250X)	866 (433X)	143 (143X)	0.5 (1X)
PI3Kδ human whole blood CD63+	3	14	15	n/a
PI3Kβ (fold vs. PI3Kδ)	87 (109X)	293 (147X)	8 (8X)	3.7 (5X)

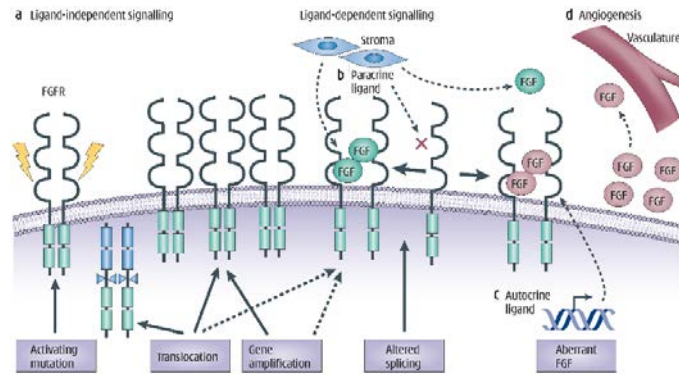
[1] AbbVie ended collaboration with Infinity in June 2016 following Phase II results in indolent non-Hodgkin's lymphoma. Duvelisib now licensed to Verastem; [2] Accelerated approval was granted based on ORR, and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trials.

# HMPL-453 - Phase I in China ongoing

## Designed as first-in-class FGFR1/2/3 inhibitor

### 1. FGFR genetic alterations are oncogenic drivers.

- FGF/FGFR signaling normally involved in embryonic development, tissue repair, angiogenesis, neuroendocrine and metabolism homeostasis.
- Multiple oncogenic driver genetic alterations in FGFR pathway: gene amplification, mutation, translocation, fusion, splicing, etc.

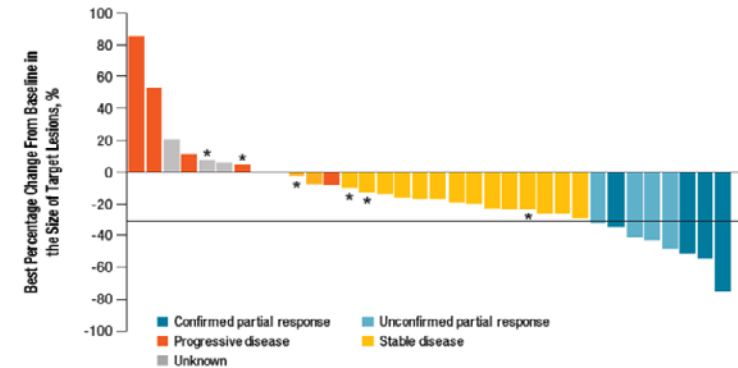


### 2. FGFR - diverse & complicated genetic changes with multiple tumor types harboring low incidence.

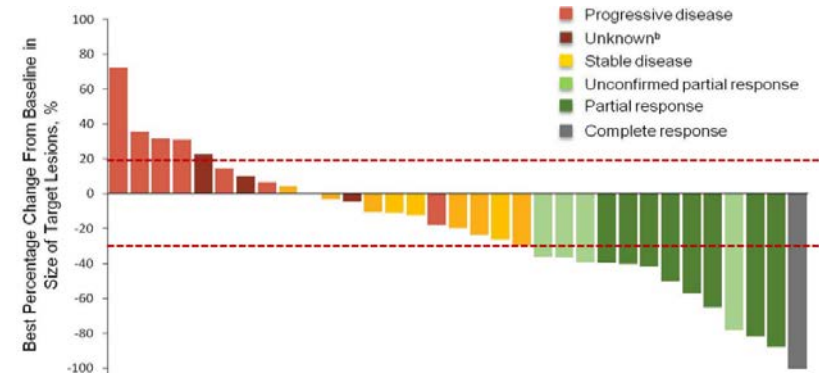
	Gene amplification	Gene translocation	Gene mutation
FGFR1	Lung squamous (7~15%) H&N squamous (10~17%) Esophageal squamous (9%) Breast (10~15%)	Lung squamous (n/a) Glioblastoma (n/a) Myeloproliferative syndrome (n/a) Breast (n/a)	Gastric (4%) Pilocytic astrocytoma (5~8%)
FGFR2	Gastric (5~10%) Breast (4%)	Intra-hepatic biliary tract cancer (cholangiocarcinoma) (14%) Breast (n/a)	Endometrial (12~14%) Lung squamous (5%)
FGFR3	Bladder (n/a) Salivary adenoid cystic (n/a)	Bladder (3~6%); Lung squamous (3%); Glioblastoma (3%) Myeloma (15~20%)	Bladder (60~80% NMIBC; 15~20 MIBC) Cervical (5%)

### 3. Biliary Tract Cancer (cholangiocarcinoma) and bladder cancer have made much progress in clinic to date.

- BJJ398 Phase II PoC in biliary tract cancer (2016 ASCO GI).



- BJJ398 Phase II PoC in bladder cancer (2016 ASCO).





## China Commercial Platform

*Providing cash generation to fund R&D in Innovation Platform*

*Established high-performance pan-China pharma sales organization*

# A powerful Rx Commercial Platform in China....

Chi-Med management run all day-to-day operations



- National Coverage:  
Over 300 cities & towns.  
~22,900 hospitals.  
~106,000 doctors.
- Medical reps. covering CV & CNS nationally.

**~2,400 RX Sales People**

**WEST**  
Pop'n: 100m (7%)

CV Medical Reps:	70 (3%)
CNS Medical Reps:	5 (5%)
HSP Sales staff:	0 (0%)

**SOUTHWEST**  
Pop'n: 190m (14%)

CV Medical Reps:	128 (6%)
CNS Medical Reps:	9 (8%)
HSP Sales staff:	0 (0%)

**NORTH**  
Pop'n: 320m (23%)

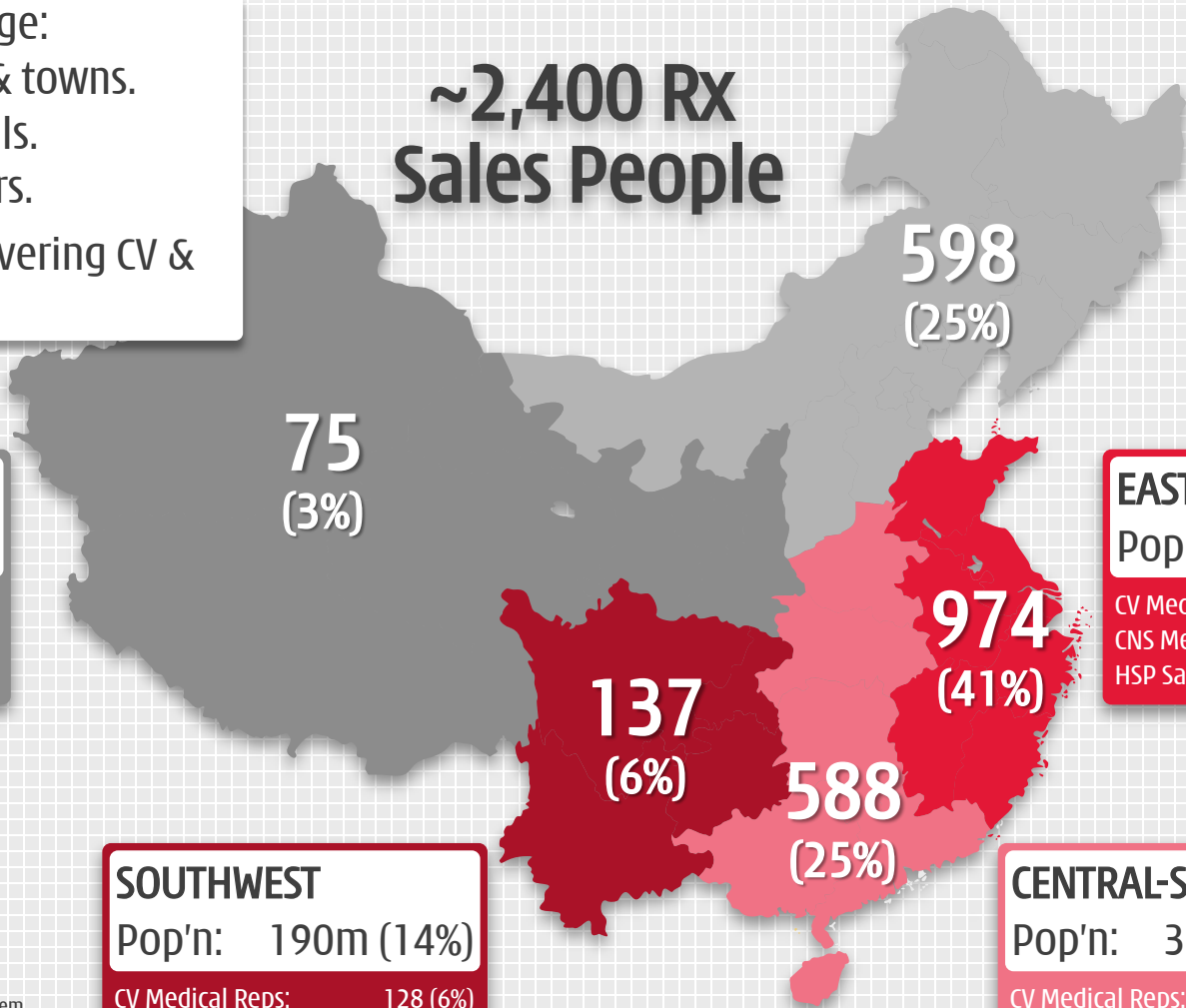
CV Medical Reps:	578 (26%)
CNS Medical Reps:	20 (19%)
HSP Sales staff:	0 (0%)

**EAST**  
Pop'n: 393m (28%)

CV Medical Reps:	896 (40%)
CNS Medical Reps:	47 (44%)
HSP Sales staff:	31 (100%)

**CENTRAL-SOUTH**  
Pop'n: 383m (28%)

CV Medical Reps:	562 (25%)
CNS Medical Reps:	26 (24%)
HSP Sales staff:	0 (0%)










Notes: 2010 Population - China State Census;  
CV = Cardiovascular; CNS = Central nervous system.  
Chi-Med Rx sales team data = 30 June 2018

# Deep portfolio of household name drugs



Top 7 products represent 71% of sales<sup>[1]</sup> and 90% of gross profit<sup>[1]</sup>

Main Products <sup>[2]</sup> - SALES (Non-GAAP)	2012	2013	2014	2015	2016	2017	H1 2017	H1 2018
 <p><b>SXBX pill</b> Coronary artery disease (Rx) 15.4% National market share Patent expiry 2029</p>	102,215 +29%	123,587 +21%	138,848 +12%	159,326 +15%	195,371 +23%	209,246 +7%	110,384 +0%	129,806 +18%
 <p><b>Banlangen granules</b> Anti-viral/flu (OTC) 53% National market share</p>	65,381 +14%	72,300 +11%	55,573 -23%	54,793 -1%	56,664 +3%	59,898 +6%	28,253 -12%	37,899 +34%
 <p><b>FFDS tablet</b> Angina (OTC) 38% National market share</p>	60,181 +6%	69,996 +16%	76,297 +9%	60,154 -21%	59,906 0%	58,936 -2%	36,059 -4%	32,767 -9%
 <p><b>Seroquel tablets</b> Bi-polar/Schizophrenia (Rx) 6% National market share</p>	n/a	n/a	n/a	21,131	34,380 +63%	35,359 +3%	18,900 +10%	16,993 <sup>[3]</sup> -10%
 <p><b>NXQ tablet</b> Cerebrovascular disease (OTC) Proprietary formulation</p>	6,933 +85%	10,142 +46%	14,681 +45%	17,581 +20%	21,000 +19%	20,408 -3%	8,744 -6%	17,026 +95%
 <p><b>KYQ granules</b> Periodontitis (OTC) &gt;90% National market share</p>	16,351 +6%	16,318 0%	18,370 +13%	17,051 -7%	17,210 +1%	17,620 +2%	7,707 -23%	10,820 +40%
 <p><b>Danning tablet</b> Gallbladder/stone (Rx) Patent expiry 2027</p>	11,648 +17%	12,364 +6%	13,822 +12%	13,526 -2%	9,041 -33%	16,089 +78%	8,762 +62%	9,510 +9%

[1] Based on aggregate Non-GAAP sales and gross profit of consolidated subsidiaries and non-consolidated joint ventures of Commercial Platform, please see appendix "Non-GAAP Financial Measures and Reconciliation"; [2] Rx = prescription drug; OTC = over-the-counter drug; SXBX pill = She Xiang Bao Xin pill; FFDS tablet = Fu Fang Dan Shen tablet; NXQ tablet = Nao Xin Qing tablet; KYQ granules = Kou Yan Qing granules; Market shares according to Frost & Sullivan or QuintilesIMS; [3] From October 2017, the majority of sales changed to a fee-for-service model due to the CNDA Two-invoice policy. Net service fee increased by 75% from H1 2017: \$5.5m to H1 2018: \$9.6m.

(US\$'000)  
(Growth % vs. Year Ago)

# Appendices

# Experienced pharma management team

POSITION	EXPERIENCE (yrs) Industry / Chi-Med	ROLE / BACKGROUND
<b>CHRISTIAN HOGG, BSc, MBA</b> <i>Chief Executive Officer</i>	 Procter & Gamble 29 / 18	Led all aspects of the creation, implementation & management of Chi-Med's strategy, business & IPOs since 2000 start - incl. AZ, Lilly, Nestlé deals & est. of pharma business.
<b>WEIGUO SU, PHD</b> <i>EVP, Chief Scientific Officer</i>	 Pfizer 28 / 13	Created Chi-Med's R&D strategy, innovation platform & led all pipeline discovery; Director of Med Chem at Pfizer; Harvard Ph.D./post-doc under Nobel Laureate E. J. Corey.
<b>JOHNNY CHENG, BEC, CA</b> <i>Chief Financial Officer</i>	 Bristol-Myers Squibb Nestlé KPMG 29 / 10	Former VP, Finance at BMS China; 8 years with Nestlé China heading finance & control in multiple businesses; KPMG & PWC in Australia & Beijing.
<b>MAREK KANIA, MD, MBA</b> <i>SVP, Chief Medical Officer, US</i>	 Lilly 25 / 1	Leads clinical development and regulatory activities outside Asia; 25 years with Lilly leading teams on oncology products incl. Erbitux, Alimta and Gemzar; former anesthesiologist & critical care physician.
<b>ZHENGPING WU, PHD, MBA</b> <i>SVP, Pharmaceutical Sciences</i>	 Roche Pfizer 24 / 10	Leads all CMC development & manufacturing for Chi-Med's pipeline; Sr Director of PS at Phenomix; Director of Pharma Development at Pfizer San Diego; at Roche in Palo Alto.
<b>MAY WANG, PHD</b> <i>SVP, Bus. Dev. &amp; Strategic Alliances</i>	 Lilly 24 / 8	Leads alliance mgmt & BD for Chi-Med; long career in research, primarily biology, strategic alliance management, partnering & business development with Eli Lilly.
<b>MARK LEE, BEng, MBA</b> <i>SVP, Corp. Finance &amp; Development</i>	 CREDIT SUISSE 19 / 9	Focuses on strategic management, overall corporate operations & alliance support; Former US/UK banker advising & raising capital for major pharma & biotech.

- **Management team comprised mainly of returnees** averaging ~20 years in multinational pharma & biotech.
- Scientific leadership have **participated in the discovery & development of global blockbusters.**



# A Risk-Balanced Global-Focused Biotech

## Innovation Platform

*Deep late-stage pipeline*

- ✓ 8 oncology drug candidates worldwide.
- ✓ 1<sup>st</sup> positive Ph.III result - fruquintinib - Launch 2018<sup>[1]</sup>
- ✓ 7 registration studies underway/completed, with 4 more set to start by mid 2019.
- ✓ ~390-person Scientific Team.

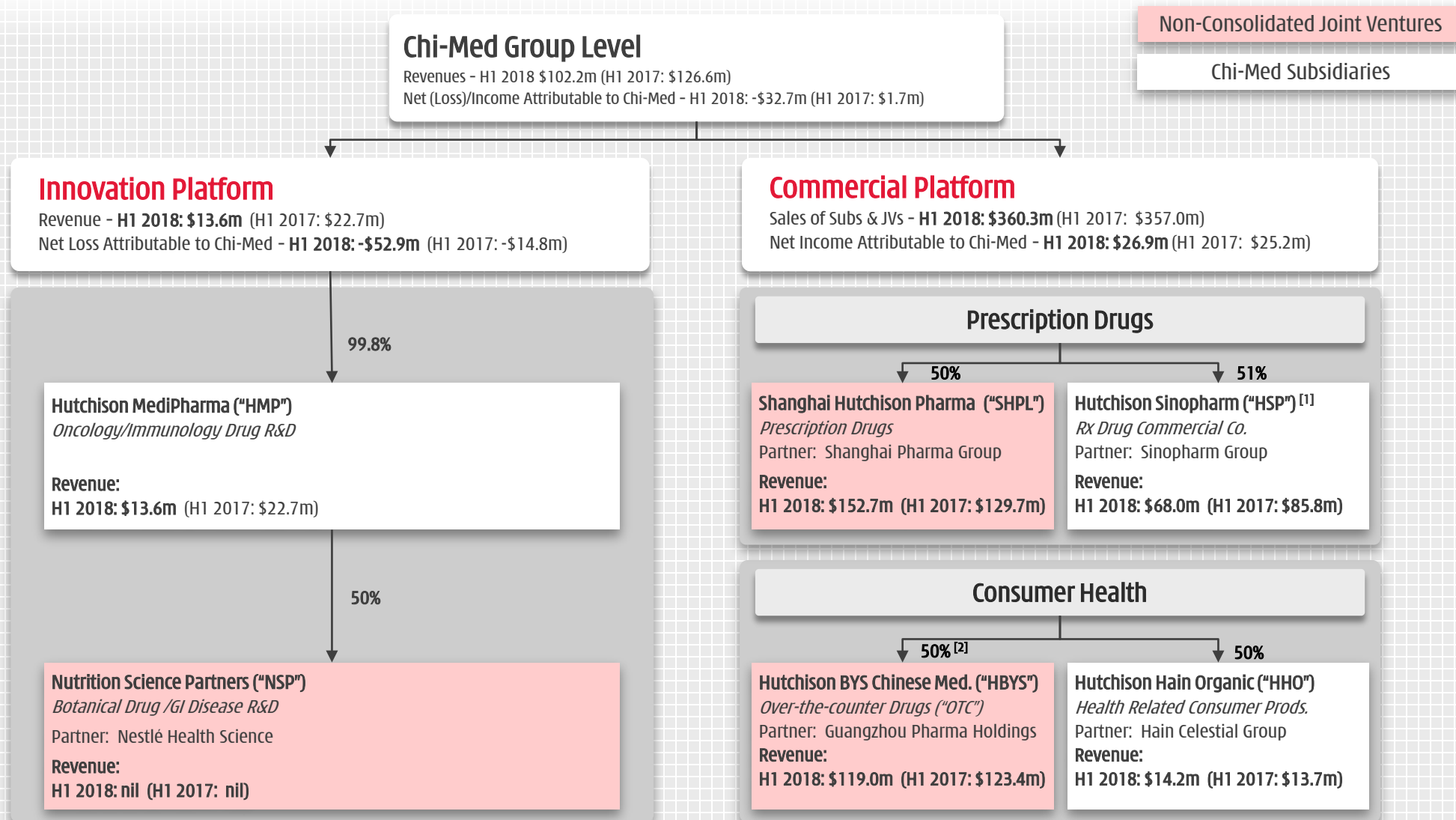
## Commercial Platform

*Solid cash flow from operations*

- ✓ ~3,400-person China Sales Team (~2,400 med. reps).
- ✓ To commercialize Innovation Platform drugs in China.<sup>[1]</sup>
- ✓ H1 2018 sales (non-GAAP)<sup>[2]</sup> up 10% to \$360.3 million.
- ✓ H1 2018 net income<sup>[3]</sup> up 19% to \$26.9 million.<sup>[4]</sup>

[1] If approved and expected; [2] H1 2018 sales (non-GAAP) represents the sum of (i) the H1 2018 GAAP revenue from external customers of our Commercial Platform (\$88.6 million), (ii) the H1 2018 revenue of our non-consolidated joint venture Shanghai Hutchison Pharmaceuticals Limited ("SHPL") (\$152.7 million) and (iii) the H1 2018 revenue of our non-consolidated joint venture Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited ("HBYS") (\$119.0 million). Excludes sales of GuanBao in H1 2017 (\$29.0 million) due to divestiture of GuanBao in Sept 2017; [3] Net income attributable to Chi-Med (non-GAAP); [4] Excludes the share of a one-time gain from SHPL's R&D related subsidies (\$2.5 million) for H1 2017.

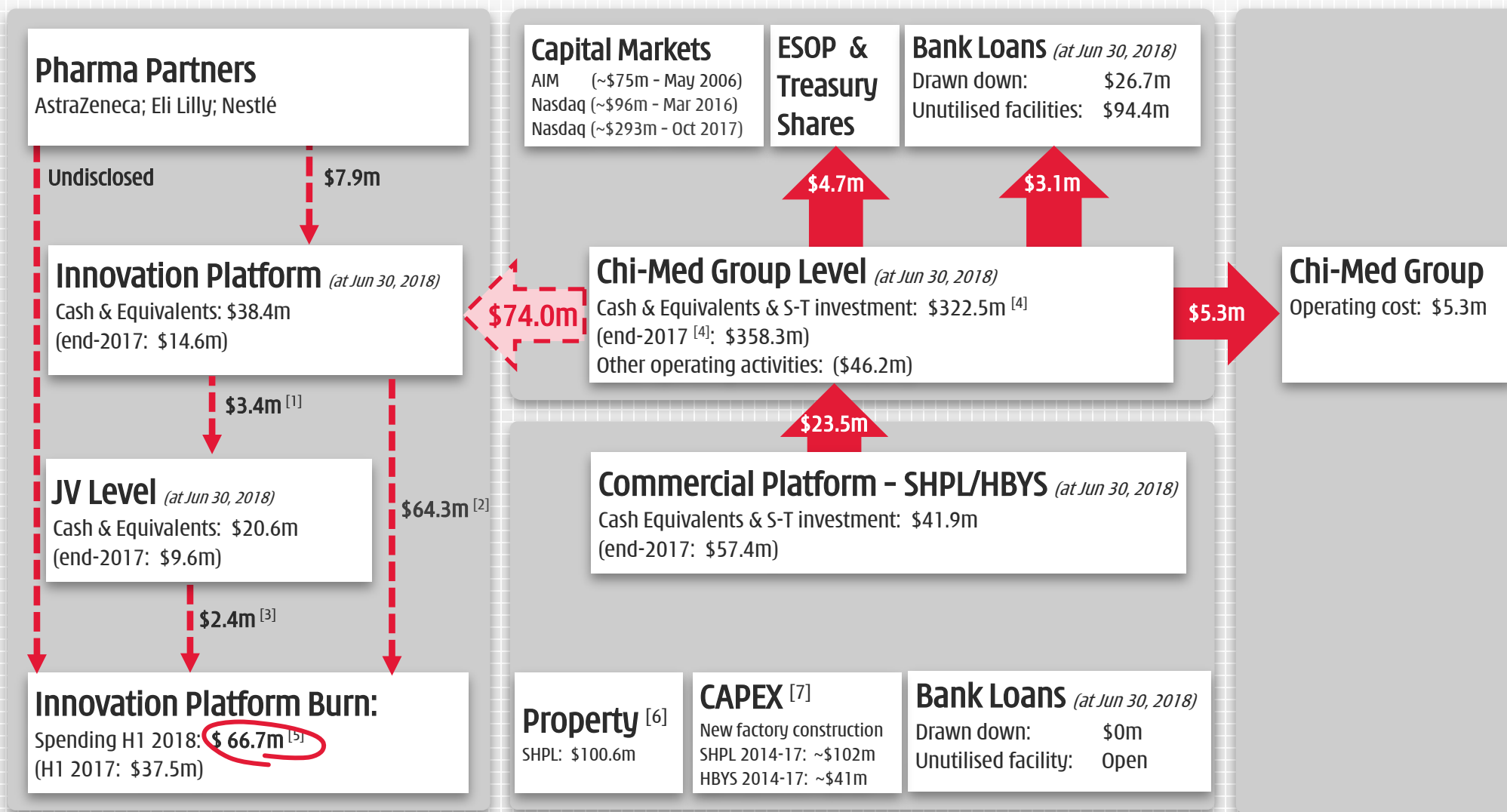
# Chi-Med Group structure - major entities



[1] Excluded HSP's ZLT business; [2] Held through an 80% owned subsidiary.

# Inter-group cash flow

\$322.5m cash (Jun 30, 2018); \$94.4m in undrawn bank facilities



[1] \$8.0m capital injection to NSP offset by \$4.6m service income received from NSP; [2] Including research & development cost and general & admin. expenses; [3] Share of NSP operating loss; [4] Including \$247.2m short-term investment (91-183 day deposit) as at end of June 2018; [5] Please see appendix "Non-GAAP Financial Measures and Reconciliation" for a Reconciliation of GAAP to adjusted research and development expenses; [6] Cash received for SHPL land compensation; [7] CAPEX required to build new Shanghai (SHPL) and Bozhou (HBYS) factories.



# Three collaborations have major aggregate financial impact



AstraZeneca 

*Lilly*



## ~\$1.2 billion in Partner payments to HMP/NSP<sup>[1]</sup>:

- \$143.5 million in upfront /milestone payments and equity injections as at Jun 30, 2018.
- up to \$340 million in further development and approvals milestones.
- up to \$145 million in option payments.
- up to \$560 million in commercial milestones.
- customary tiered royalties on net sales.

## Clinical trial spending<sup>[2]</sup>:

- clinical costs for partnered drug candidates estimated at several hundred million US dollars.
- Partners to fund the majority of these clinical costs.

## Possible payment events in H2 2018/H1 2019:

- Fruquintinib: NDA approval for third line CRC.<sup>[3]</sup>
- Savolitinib: Start of Phase III in NSCLC.<sup>[4]</sup>

[1] Nutrition Science Partners Limited ("NSP") is the 50/50 joint venture between Nestlé Health Science ("Nestlé") and Chi-Med; [2] includes clinical and direct non-clinical costs;

[3] CRC = Colorectal Cancer; [4] NSCLC = non-small cell lung cancer, and subject to regulatory discussions.

# Major market potential

		Pot. launch Year / Territory	Incidence (New pts./yr.) <sup>[1]</sup>	Approx. WAC <sup>[2]</sup> of various reference TKIs (US\$/month)	Median PFS (months) <sup>[3]</sup>	Potential Peak (US\$) <sup>[4]</sup>	
						Sales	Net Income
SAVO	Papillary renal cell carcinoma (c-Met-driven)	2020/21 Global	~25,000	\$11,600 (Sutent®) \$10,500 (Afinitor®)	6.2 Ph.II	~\$110-160m @est. 20-25% penetration <sup>[5]</sup>	~\$20-35m @15-20% tier royalty/other
	NSCLC -2L 1 <sup>st</sup> Gen EGFR TKI refract, Tagrisso combo (MET+ , T790M+/-)	2022 Global	~35,000 - 40,000	\$15,100 (Tagrisso®)	TBD		
	NSCLC -2L/3L 3 <sup>rd</sup> Gen EGFR TKI refract. Tagrisso combo (MET+)	2021 Global	TBD	\$15,100 (Tagrisso®)	TBD		
	NSCLC -1L MET EXON14m/deletion	2021 China	TBD	\$15,100 (Tagrisso®) (China price ~\$7,000)	TBD		
FRUQ	3L (or above) Colorectal cancer ("CRC")	2018 China	~50,000 - 60,000	\$14,000 (Regorafenib - global) \$2,870 (Apatinib - China off label)	3.7 Ph.III		
	3L Non-small cell lung cancer ("NSCLC")	2019 China	~60,000 - 70,000	No approved TKIs \$2,870 (Apatinib - China off label)	3.8 Ph.II		
	2L Gastric cancer combo with Taxol	2020 China	~250,000 - 300,000	\$2,870 (Apatinib appr. 3L Gastric) \$1,810 (Apatinib NDRL <sup>[7]</sup> reimbursed)	3.7 Ph.II		
SULF	Pancreatic neuroendocrine tumors	2020 China	~5,000 - 6,000	\$11,000 (Sutent®/Afinitor® - global) \$5,500 (Somatuline® - global)	19.4 Ph.II		
	Non-pancreatic neuroendocrine tumors	2020 China	~50,000 - 60,000	\$11,000 (Sutent®/Afinitor® - global) \$2,190 (Afinitor® China NDRL) \$5,500 (Somatuline® - global)	13.4 Ph.II		
	2L chemo-refractory biliary tract cancer ("BTC")	2020/21 China	~30,000 - 35,000	No approved TKIs	TBD		
EPIT	1L EGFR-mutant NSCLC with brain metastasis	2020/21 China	~30,000 - 40,000	\$15,100 (Tagrisso®) - Brain pen. <sup>[6]</sup> \$1,100 (Iressa®) - min. brain pen. \$850 (Conmana®) - min. brain pen.	TBD		

[1] Addressable Patient Population = Company estimates considering Frost & Sullivan data, National Central Cancer Registry of China and publicly available epidemiology data; [2] WAC = Wholesaler Acquisition Cost; [3] Last published median Progression-Free Survival ("PFS" or time to >20% tumor growth) result for Chi-Med therapy (Chi-Med studies); [4] Company estimates; [5] Penetration = % of Addressable Patients treated for an average period equivalent to the median PFS; [6] Tagrisso received approval in China in 2017; [7] NDRL = National Drug Reimbursement List.

# National Drug Reimbursement List Pricing ("NDRL")

July'17 update - 15 new drugs in oncology<sup>[1]</sup> added to NDRL

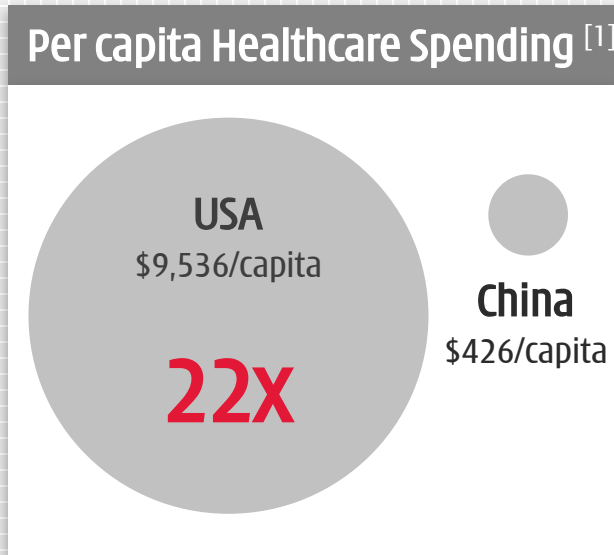


Brand (generic)	Company	Unit Pricing (US\$) <sup>[3]</sup>				Approximate Monthly Pricing (US\$) <sup>[3]</sup>			Indication coverage
		Dosage	Avg. Tender	Reimbursed	Δ%	Dosage	Avg. Tender	Reimbursed	
<b>Herceptin®</b> (trastuzumab)	Roche	440mg:20ml	\$3,298.81	\$1,125.93	-66%	Breast: 4mg/kg wk 1, 2mg/kg weekly. <sup>[2]</sup>	\$4,500	<b>\$1,540</b>	Breast: Her2+; Her2+ meta. Her2+ late-stage meta. gastric.
<b>Avastin®</b> (bevacizumab)	Roche	100mg:4ml	\$772.74	\$296.00	-62%	10mg/kg Q2W.	\$11,590	<b>\$4,440</b>	Late-stage meta. CRC or advanced non-squamous NSCLC.
<b>TheraCIM®<sup>[4]</sup></b> (nimotuzumab)	Biotech Pharma	50mg:10ml	\$435.26	\$251.85	-42%	100mg weekly.	\$3,730	<b>\$2,160</b>	Combo with radiotherapy for EGFR+ Stage III/IV nasopharyngeal carcinoma.
<b>Rituxan®</b> (rituximab)	Roche	500mg:50ml <sup>[2]</sup>	\$2,544.74	\$1,228.15	-52%	375 mg/m <sup>2</sup> weekly.	\$13,090	<b>\$6,320</b>	Restorative or resistant follicular central type lym.; CD20+ stage III-IV follicular NHL, CD20+ DLBCL.
<b>Tarceva®</b> (erlotinib)	Roche	150mg <sup>[2]</sup>	\$68.15	\$28.89	-58%	150mg QD.	\$2,040	<b>\$870</b>	Advanced NSCLC with limited EGFR gene mutation.
<b>Nexavar®</b> (sorafenib)	Bayer	0.2g	\$60.44	\$30.07	-50%	400mg BID.	\$7,250	<b>\$3,610</b>	Unresectable RCC. Unresectable HCC. meta. Diff. thyroid after radio-iodine therapy.
<b>Tykerb®</b> (lapatinib)	GSK	250mg	\$17.63	\$10.37	-41%	1,500mg QD.	\$3,170	<b>\$1,870</b>	Adv./meta. breast cancer with Her2 O/E, after anthracycline, paclitaxel, trastuzumab.
<b>AiTan®</b> (apatinib)	Hengrui	425mg <sup>[2]</sup>	\$47.85	\$30.22	-37%	850mg QD.	\$2,870	<b>\$1,810</b>	3L gastric adenocarcinoma or esophageal junction with adenocarcinoma.
<b>Velcade®</b> (bortezomib)	J&J	3.5mg <sup>[2]</sup>	\$1,873.78	\$906.07	-52%	1.3mg/m <sup>2</sup> quartic every 3 wks.	\$6,360	<b>\$3,080</b>	Myeloma; recurring or refractory mantle cell lymphoma.
<b>EnDu®</b> (rh-endostatin)	Simcere	15mg	\$132.15	\$93.33	-29%	7.5mg/m <sup>2</sup> iv QD 2-wks-on / 1-week-off.	\$2,110	<b>\$1,490</b>	Late-stage NSCLC.
<b>Epidaza®</b> (chidamide)	Chipscreen	5mg	\$81.48	\$57.04	-30%	30mg QD, 2x per wk.	\$4,190	<b>\$2,930</b>	2L+ Recurring or refractory peripheral T-cell lymphoma (PTCL).
<b>Zytiga®</b> (abiraterone)	J&J	250mg	\$45.63	\$21.48	-53%	1,000mg QD.	\$5,480	<b>\$2,580</b>	Metastatic or ovariectomized prostate cancer.
<b>Faslodex®</b> (fulvestrant)	AstraZeneca	250mg:5ml	\$806.81	\$355.56	-56%	500mg per month.	\$1,610	<b>\$710</b>	Advanced ER/PR+ breast can., failing aromatase inhibitor.
<b>Afinitor®</b> (everolimus)	Novartis	5mg <sup>[2]</sup>	\$36.44	\$21.93	-40%	10mg QD.	\$2,190	<b>\$1,320</b>	Adv. RCC after sunitinib or sorafenib. Adv./meta. pancreatic NETs. Tuberous sclerosis with renal angiomyolipoma.
<b>Revlimid</b> (lenalidomide)	Celgene	25mg <sup>[2]</sup>	\$413.93	\$163.26	-61%	25mg QD 3-wks-on / 1-wk-off.	\$9,310	<b>\$3,670</b>	2L+ Recurring myeloma.

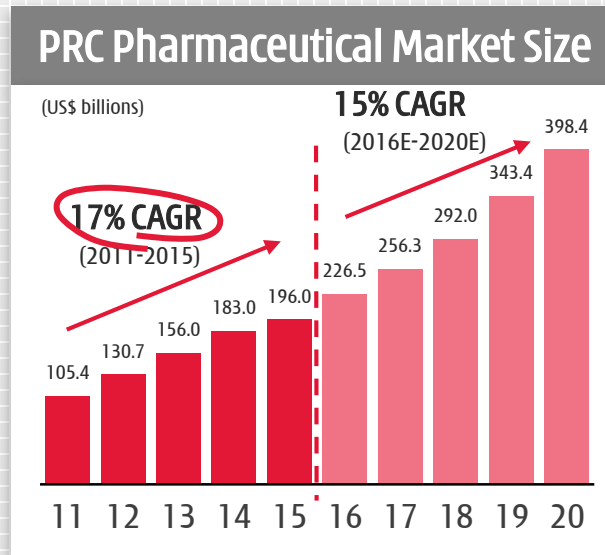
Source: Ministry of Human Resources and Social Security (MOHRSS); Yaozhi; BofA Merrill Lynch Global Research.

[1] Excluding 3 botanical oncology drugs; [2] Reference SKU or reference recommended dosage for monthly pricing calculation; [3] Calculation assumes an exchange rate of CN¥6.75 per US\$1; [4] Marketed as Tai Xin Sheng® in China.

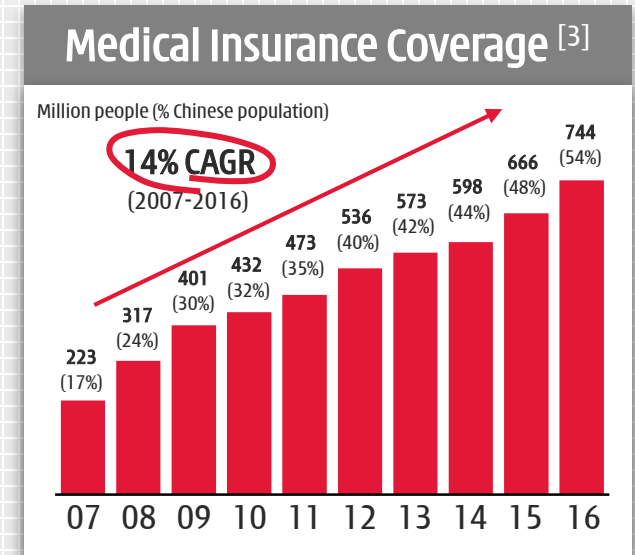
# China pharma market has become the second largest globally since 2016



Source: WHO Global Health Expenditure Database (2015 data).



Source: Frost & Sullivan.



Source: National Bureau of Statistics (2016).

- China pharmaceutical industry growth 17% CAGR from 2011-2015 - one of the higher rated industries in China with average P/E ratio of 40 for the 61 listed companies (next slide).
- Government healthcare spending grew 14% CAGR<sup>[2]</sup> from 2011-2015 and continues to increase rapidly - Strategic priority.
- Expansion of State Medical Insurance Schemes - Link to increased drug reimbursement & sales.

[1] Current health expenditure by revenues of health care financing schemes (in current US\$ per capita); [2] National Bureau of Statistics of China; [3] Urban Basic Medical Care Insurance - total persons covered at year-end  
CAGR = Compound annual growth rate

# China Commercial Platform has substantial value

- Chi-Med's Commercial Platform continues to perform well relative to our peer group.
- The market value, based on China Pharma PE multiples is approximately \$2.9 - 3.1 billion.<sup>[1]</sup> Given our share in the JVs, Chi-Med's share of this value is approximately **\$1.4 - 1.5 billion**.

	Code	NET SALES			NET INCOME				VALUATION <sup>[3]</sup>	
		2016 Jan-Dec	2017 Jan-Dec	FY16-17 Growth	2016 Jan-Dec	2017 Jan-Dec	FY16-17 Growth	FY2017 Margin	Market Cap.	P/E
<b>CHI-MED Commercial Platform -- Subsidiaries/JVs<sup>[2]</sup></b>		<b>627.4</b>	<b>677.2</b>	<b>8%</b>	<b>63.3</b>	<b>77.3</b>	<b>22%</b>	<b>11%</b>	<b>n/a</b>	<b>n/a</b>
Tianjin Zhong Xin Pharma	600329	925.0	851.7	-8%	61.0	70.8	16%	8%	2,039	22
Li Zhu Pharma	000513	1,145.5	1,277.1	11%	102.0	122.8	20%	9.6%	4,727	38
Shandong Dong E E Jiao	000423	945.7	1,103.6	17%	277.7	306.0	10%	28%	5,242	20
Zhejiang Kang En Bai Pharma	600572	901.3	792.5	-12%	60.5	109.3	81%	14%	3,046	23
Kunming Pharma	600422	763.6	876.1	15%	61.3	50.2	-18%	6%	972	25
Guizhou Yi Bai Pharma	600594	551.9	570.0	3%	58.9	61.0	4%	11%	1,069	23
Jin Ling Pharma	000919	535.7	477.8	-11%	33.3	25.9	-22%	5%	573	30
Jiangsu Kang Yuan	600557	449.1	490.2	9%	56.3	56.6	1%	12%	1,136	22
Zhuzhou Qian Jin Pharma	600479	428.9	476.5	11%	26.0	36.9	42%	8%	651	26
ZhangZhou Pian Zai Huang	600436	345.7	556.0	61%	75.9	116.8	54%	21%	11,196	55
<b>Peer Group -- Weighted Avg. (10 Comps. excl. Chi-Med)</b>		<b>699.2</b>	<b>747.2</b>	<b>7%</b>	<b>81.3</b>	<b>95.6</b>	<b>18%</b>	<b>13%</b>	<b>3,065</b>	<b>37</b>
<b>All 61 Listed China Pharma. Companies -- Weighted Average</b>		<b>1,155.1</b>	<b>1,270.1</b>	<b>10%</b>	<b>96.0</b>	<b>123.5</b>	<b>29%</b>	<b>10%</b>	<b>3,533</b>	<b>40</b>

Peer Group: 10 companies (excl. Chi-Med) selected as ALL listed and profitable mainland Chinese OTC/RX pharma manufacturing companies, with a focus on similar product types, and FY2017 Net Sales in the ~\$400-1,300 million range.

Source: Company data, Deutsche Bank, FactSet

[1] Peer group/China Pharma multiple of 37x-40x 2017 actual Net income after tax of \$77.3 million (excluding SHPL's R&D related subsidies of US\$5.0 million at net income after tax);

[2] Total aggregate PRC domestic results of Chi-Med's 6 Commercial Platform companies (HBYS, SHPL, Hutchison Sinopharm, HHO, HHL & HCPL), excluding discontinued operations and land compensation from SHPL;

[3] Market Capitalization and Price Earnings Ratios as at **July 19, 2018**: Trailing Twelve Month PE weighted averaged based on market capitalization.

(US\$ millions)

# Innovation Platform proxy peer group (1/2)

## A very deep pipeline and a very large organization/operation

Name	Mkt Cap (July 16)			Ent. Value <sup>[1]</sup>	Staff	Overview of pipeline assets												
	2018	2017	2016			Drug	Studies	Phase	Partner	# of drugs	# of studies							
										P3	P2	P1						
<b>Genmab</b>	10,521	13,454	10,170	9,564	263	Arzerra (ofatumumab)	CLL, FL	Mktdd, P3	Novartis	13	13	6	14					
						Ofatumumab (subcutaneous)	Relapsing multiple sclerosis	2xP3	Novartis									
						Darzalex (daratumumab)	MM, amyloidosis, NKT-cell lym., myelodysplastic syndromes, solid tumors	Mktdd, Reg., 9xP3, 3xP2, 5xP1	Janssen									
						Teprotumumab (RV001)	Graves' orbitopathy (thyroid eye disease)	P3	Horizon									
						Tisotumab vedotin	Solid tumors	1xP2, 2xP1/2	Seattle Genetics									
						HuMax-AXL-ADC, HexaBody-DR5/DR5	Solid tumors	1xP1/2 (ongoing), 1xP1/2 (to start in 2018)										
						DuoBody-CD3xCD20	Hematological malignancies	P1/2 (to start in 1H2018)										
						AMG 714	Celiac disease	2xP2	Amgen									
						ADCT-301, JNJ-61186372, JNJ-63709178, JNJ-64007957	Lym., AML, ALL, NSCLC, R/R MM	5xP1	ADC, Janssen									
	<b>BelGene</b>	8,773	2,941	972	7,480	900	BGB-3111; BGB-3111 + Gazyva	WM, 1L CLL, R/R MCL, R/R CLL, R/R DLBCL, R/R FL	2xP3, 4xP2						7	6	7	10
							BGB-A317	2L NSCLC, 1L hepatocellular carcinoma, R/R Hodgkin's lym. 2L+ UC	4xP3, 2xP2					Celgene				
						BGB-290	3L gBRCA+ ovarian cancer	P1, P2										
						BGB-283	BRAF and RAS mutated solid tumors	2xP1										
						BGB-A317 + BGB-290; BGB-A317 + BGB-3111	Solid tumors; B-cell malignancies	2xP1										
						BGB-290 +(RT)/Chemo; BGB-A333 +/- BGB-A317	Solid tumors, glioblastoma	3xP1										
						CC-122	R/R DLBCL, NHL	P1										
						Sitravatinib	NSCLC	P1	Mirati									
<b>Exelixis</b>	6,255	7,822	1,931	5,828	372	Cabometyx / Cometriq (cabozantinib)	Thyroid cancer, advanced renal CC, adv. hepatocellular carcinoma, NSCLC, genitourinary tumors, endometrial cancer, breast cancer & others	Mktdd, 2xP3, 14xP2, 5xP1	Ipsen, Takeda	6	7	22	8					
						Cotellic (cobimetinib)	Metastatic or unresectable locally advanced melanoma, CRC, BC, pancreatic cancer	Mktdd, 3xP3, 2xP2, P1	Genentech									
						Esaxerenone (CS-3150)	Hypertension, diabetic nephropathy	2xP3	Daiichi Sankyo									
						SAR245408 (XL147)	Variety of cancer indications	P2	Sanofi									
						SAR245409 (XL765)	NHL, glioblastoma, lym., BC, leukemia, combos w/ Treanda, Rituxan	5xP2	Sanofi									
						XL888	BRAF V600 Mutation-Pos advanced melanoma, Malignant melanoma	2xP1										
<b>Loxo</b>	5,263	2,180	551	4,553	73	Larotrectinib (LOXO-101)	Cancers Harboring Alterations of TRK	Reg., 2xP2, 2xP1	Bayer	3	0	2	4					
						LOXO-292	Cancers Harboring Alterations of RET	P1										
						LOXO-195	Next-Gen TRK inhibitor for potential acquired resistance	P1	Bayer									
<b>Aglos</b>	5,185	2,787	1,583	4,403	382	Ihdifa; + Vidaza; + (7+3)	R/R AML, frontline AML	Mktdd., P3, 2xP2	Celgene	5	4	3	7					
						Ivosidenib; + Vidaza; + (7+3); + AG-881	Frontline AML, R/R AML, cholangiocarcinoma, low grade glioma	Reg., 3xP3, 5xP1	-									
						AG-348	PK deficiency	P2										
						AG-270	MTAP-deleted tumors	P1	-									
						AG-881	Low grade glioma	P1	Celgene									

Source: Deutsche Bank, Company data, FactSet, public filings

[1] As of July 16, 2018

Key: CLL = chronic lymphocytic leukemia; Lym. = lymphoma; NHL = Non-Hodgkin's Lymphoma; AML = acute myeloid leukemia; ALL = acute lymphoblastic leukemia; WM = Waldenstrom's macroglobulinemia; MCL = mantle cell lymphoma; FL = follicular lymphoma; DLBCL = diffuse large B-cell lymphoma; RA = Rheumatoid Arthritis; MM = Multiple Myeloma; CC = Cell Carcinoma; NSCLC = Non-Small Cell Lung Cancer; BC = Breast Cancer; CRC = colorectal cancer; CD = Crohn's disease; R/R = relapsed / refractory; Mktdd = Marketed; Reg. = Under Registration.

(\$ millions unless otherwise stated)

# Innovation Platform proxy peer group (2/2)

## A very deep pipeline and a very large organization/operation

Name	Mkt Cap (July 16)			Ent. Value <sup>[1]</sup>	Staff	Drug	Overview of pipeline assets			# of drugs	# of studies		
	2018	2017	2016				Studies	Phase	Partner		P3	P2	P1
Galapagos	5,234	3,916	2,426	3,871	600	Filgotinib	RA, CD, UC, small bowel CD, Fistulizing CD, Sjogren's, ankylosing spondylitis, psoriatic arthritis, cutaneous lupus, lupus nephropathy, uveitis	3xP3, 8xP2	Gilead	11	3	11	5
						'2222; '2222 + Kalydeco	Cystic fibrosis	2xP2, 3xP1	AbbVie				
						'2451 + '2222 + '2737;							
						'3067 + '2222 + '2737;							
						'3067 + '2222 + '3221;							
Morphosys <sup>[2]</sup>	4,063	2,243	1,151	3,671	310	MOR208	CLL, SLL, DLBCL	P3, 2xP2		3	1	3	1
						MOR202	Multiple myeloma	P2					
						MOR107	Undisclosed	P1					
Array <sup>[2]</sup>	3,587	1,468	531	3,256	209	ARRY-797	LMNA-related DCM	P2	-	2	0	2	0
						ARRY-382	Solid tumors	P2	-				
Clovis	2,414	4,458	552	2,256	360	Rubraca (rucaparib); + nivolumab; + atezolizumab	Advanced ovarian cancer, ovarian cancer treat./maint., prostate, triple negative BC, BC, gastro esophageal, gynecological	Mktd, Reg., 4xP3, 3xP2, P1		1	4	3	1
Tesaro	2,223	6,796	4,408	2,165	715	Varubi (IV and oral)	CINV (oral and IV)	Mktd, Reg.	Opko, Tersera	5	1	5	6
						Zejula (niraparib); + anti-PD-1	Ovarian cancer maintenance, ovarian cancer treatment, NSCLC	Mktd, Reg., P3, 2xP2	Merck				
						Niraparib + Pembrolizumab	Triple-negative BC or ovarian cancer (TOPACIO study)	P2	Merck				
						Niraparib + Bevaciumab	Ovarian cancer, 1L ovarian cancer maintenance	2xP2	Roche				
						Niraparib + chemotherapy; TSR-042 (+combos); TSR-022; TSR-033	Advanced NSCLC, advanced or metastatic cancer, SCCL, Ewing's sarcoma, various tumor types	6xP1	AnaptysBio, SARC				
Puma	1,987	3,310	1,072	1,957	318	Neratinib (PB272)	Adjuvant BC, neoadjuvant BC, metastatic BC, metastatic BC wit brain met., met. her2 BC	Mktd., P3, 8xP2		1	1	8	0
<b>AVERAGE</b>	<b>5,046</b>	<b>4,670</b>	<b>2,304</b>	<b>4,455</b>	<b>409</b>					<b>5</b>	<b>4</b>	<b>7</b>	<b>5</b>
<b>MEDIAN</b>	<b>5,185</b>	<b>3,310</b>	<b>1,151</b>	<b>3,871</b>	<b>360</b>					<b>5</b>	<b>3</b>	<b>5</b>	<b>5</b>
Innovation Platform	~390					Savoltinib	PRCC, CCRCC, NSCLC, gastric cancer, lung cancer, prostate cancer	2x reg. trials, 11x PoC	AstraZeneca	8	7	21	5
						Fruquintinib	CRC, NSCLC, caucasian bridging, gastric cancer	1x reg., 2 reg. trials, 1x PoC, 1xP1	Eli Lilly				
						Sulfatinib	Pancreatic and non-pancreatic NETs, Caucasian bridging, medullary thyroid cancer, differentiated thyroid cancer, biliary tract cancer	2x reg. trials, 4x PoC					
						Epitinib	NSCLC, glioblastoma	2x PoC					
						Thellatinib	Solid tumors, esophageal cancer	1x PoC					
						HMPL-523	RA, hematological cancers, Immunology, lym.	2x PoC, 1xP1					
						HMPL-689	Hematological cancers, lym.	2xP1					
						HMPL-453	Solid tumors	1xP1					

Source: Deutsche Bank, Company data, FactSet, public filings

[1] As of July 16, 2018

[2] Only non-partnered products included for Morphosys and Array. Array also owns two products in phase 3 (Binimetinib and Encorafenib) in which Array maintains US and Canadian rights.

Key: CLL = chronic lymphocytic leukemia; Lym. = lymphoma; NHL = Non-Hodgkin's Lymphoma; AML = acute myeloid leukemia; ALL = acute lymphoblastic leukemia; WM = Waldenstrom's macroglobulinemia; MCL = mantle cell lymphoma; FL = follicular lymphoma; DLBCL = diffuse large B-cell lymphoma; RA = Rheumatoid Arthritis; MM = Multiple Myeloma; CC = Cell Carcinoma; NSCLC = Non-Small Cell Lung Cancer; BC = Breast Cancer; CRC = colorectal cancer; CD = Crohn's disease; R/R = relapsed / refractory; Mktd = Marketed; Reg. = Under Registration.

(\$ millions unless otherwise stated)

# Non-GAAP Financial Measures and Reconciliation (1/2)



## Reconciliation of Adjusted Research and Development Expenses (Page 5 and Page 80):

	H1 2018	H1 2017
Research and development expenses	(60.1)	(31.6)
Plus: Innovation Platform – administrative and other expenses	(4.3)	(3.6)
Plus: Equity in earnings of equity investees – NSP and other	(2.3)	(2.4)
Plus: Innovation Platform – interest income	0.0	0.1
<b>Adjusted research and development expenses</b>	<b>(66.7)</b>	<b>(37.5)</b>

## Reconciliation of Top 7 products' Gross Profit as Percentage of Aggregated Gross Profit for Commercial Platform (Page 75):

	H1 2018
Sales of goods – third parties and related parties	88.6
Less: Costs of sales of goods – third parties and related parties	(71.9)
<b>Consolidated gross profit</b>	<b>16.7</b>
Plus: Gross profit – HBYS and SHPL	168.0
<b>Adjusted gross profit</b>	<b>184.7</b>
<b>Top 7 products gross profit</b>	<b>166.0</b>
% of Top 7 products to adjusted gross profit	90%

(US\$ millions unless otherwise stated)



# Non-GAAP Financial Measures and Reconciliation (2/2)



## Reconciliation of Non-GAAP Sales and Non-GAAP Net (loss)/income after tax <sup>[1]</sup>

- Prescription Drugs: includes our Consolidated subsidiary (Hutchison Sinopharm) and Non-consolidated joint venture (SHPL);
- Consumer Health: includes our Consolidated subsidiaries (HHO, HHL and HCP) and Non-consolidated joint venture (HBYS).

(US\$ millions)	IFRS											US GAAP					H1'17-H1'18	
	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	H1'17	H1'18	Growth
<b>Sales (Non-GAAP)</b>	<b>21.9</b>	<b>27.9</b>	<b>65.1</b>	<b>101.4</b>	<b>119.0</b>	<b>155.8</b>	<b>197.0</b>	<b>236.4</b>	<b>278.6</b>	<b>360.7</b>	<b>402.3</b>	<b>465.4</b>	<b>518.9</b>	<b>627.4</b>	<b>677.2</b>	<b>357.0</b>	<b>360.3</b>	<b>1%</b>
<i>Prescription Drugs</i>	<i>17.2</i>	<i>21.8</i>	<i>23.3</i>	<i>23.2</i>	<i>28.1</i>	<i>39.5</i>	<i>54.4</i>	<i>71.2</i>	<i>92.4</i>	<i>116.5</i>	<i>138.2</i>	<i>204.9</i>	<i>286.6</i>	<i>372.3</i>	<i>411.0</i>	<i>215.5</i>	<i>220.7</i>	<i>2%</i>
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	50.2	105.5	149.9	166.4	85.8	68.0	-21%
- Non-consolidated joint venture	17.2	21.8	23.3	23.2	28.1	39.5	54.4	71.2	92.4	116.5	138.2	154.7	181.1	222.4	244.6	129.7	152.7	18%
<i>Consumer Health</i>	<i>4.7</i>	<i>6.1</i>	<i>41.8</i>	<i>78.2</i>	<i>90.9</i>	<i>116.3</i>	<i>142.6</i>	<i>165.2</i>	<i>186.2</i>	<i>244.2</i>	<i>264.1</i>	<i>260.5</i>	<i>232.3</i>	<i>255.1</i>	<i>266.2</i>	<i>141.5</i>	<i>139.6</i>	<i>-1%</i>
- Consolidated subsidiaries	4.7	6.1	9.3	8.9	3.7	5.5	7.0	14.1	14.9	15.5	16.5	16.8	20.7	31.0	38.8	18.1	20.6	14%
- Non-consolidated joint venture	-	-	32.5	69.3	87.2	110.8	135.6	151.1	171.3	228.7	247.6	243.7	211.6	224.1	227.4	123.4	119.0	-4%
<b>Total Sales Growth</b>	<b>n/a</b>	<b>27%</b>	<b>133%</b>	<b>56%</b>	<b>17%</b>	<b>31%</b>	<b>26%</b>	<b>20%</b>	<b>18%</b>	<b>29%</b>	<b>n/a</b>	<b>16%</b>	<b>11%</b>	<b>21%</b>	<b>8%</b>		<b>1%</b>	
- GuanBao divested in Sept 2017	-	-	-	-	-	-	-	-	(11.4)	(50.5)	(51.6)	(49.7)	(40.7)	(45.0)	(38.6)	(29.0)	-	n/a
<b>Adjusted Consumer Health excl. GuanBao</b>	<b>4.7</b>	<b>6.1</b>	<b>41.8</b>	<b>78.2</b>	<b>90.9</b>	<b>116.3</b>	<b>142.6</b>	<b>165.2</b>	<b>174.8</b>	<b>193.7</b>	<b>212.5</b>	<b>210.8</b>	<b>191.6</b>	<b>210.1</b>	<b>227.6</b>	<b>112.5</b>	<b>139.6</b>	<b>24%</b>
- Adjusted Non-consolidated joint venture	-	-	32.5	69.3	87.2	110.8	135.6	151.1	159.9	178.2	196.0	194.0	170.9	179.1	188.8	94.4	119.0	26%
<b>Adjusted Sales excl. GuanBao (Non-GAAP)</b>	<b>21.9</b>	<b>27.9</b>	<b>65.1</b>	<b>101.4</b>	<b>119.0</b>	<b>155.8</b>	<b>197.0</b>	<b>236.4</b>	<b>267.2</b>	<b>310.2</b>	<b>350.7</b>	<b>415.7</b>	<b>478.2</b>	<b>582.4</b>	<b>638.6</b>	<b>328.0</b>	<b>360.3</b>	<b>10%</b>
<b>Total Adjusted Sales Growth</b>	<b>n/a</b>	<b>27%</b>	<b>133%</b>	<b>56%</b>	<b>17%</b>	<b>31%</b>	<b>26%</b>	<b>20%</b>	<b>13%</b>	<b>16%</b>	<b>13%</b>	<b>19%</b>	<b>15%</b>	<b>22%</b>	<b>10%</b>		<b>10%</b>	
<b>Net (loss)/income attrib. to Chi-Med</b>	<b>(5.7)</b>	<b>(3.7)</b>	<b>(0.5)</b>	<b>1.2</b>	<b>4.5</b> <sup>[2]</sup>	<b>5.9</b> <sup>[2]</sup>	<b>9.3</b> <sup>[2]</sup>	<b>12.6</b> <sup>[2]</sup>	<b>13.6</b> <sup>[2]</sup>	<b>14.6</b> <sup>[2]</sup>	<b>18.2</b> <sup>[2]</sup>	<b>22.8</b> <sup>[2]</sup>	<b>25.2</b> <sup>[2]</sup>	<b>29.9</b> <sup>[3]</sup>	<b>37.5</b> <sup>[4]</sup>	<b>22.7</b> <sup>[4]</sup>	<b>26.9</b>	<b>19%</b>
<i>Prescription Drugs</i>	<i>(0.2)</i>	<i>0.6</i>	<i>1.0</i>	<i>0.7</i>	<i>0.9</i>	<i>1.4</i>	<i>3.0</i>	<i>5.9</i>	<i>7.1</i>	<i>8.8</i>	<i>11.2</i>	<i>13.2</i>	<i>15.9</i>	<i>20.7</i>	<i>26.5</i>	<i>16.9</i>	<i>20.8</i>	<i>23%</i>
<i>Consumer Health</i>	<i>(5.5)</i>	<i>(4.3)</i>	<i>(1.5)</i>	<i>0.5</i>	<i>3.6</i>	<i>4.5</i>	<i>6.3</i>	<i>6.7</i>	<i>6.5</i>	<i>5.8</i>	<i>7.0</i>	<i>9.6</i>	<i>9.3</i>	<i>9.2</i>	<i>11.0</i>	<i>5.8</i>	<i>6.1</i>	<i>7%</i>
<b>Net (loss)/income attrib. to Chi-Med growth</b>	<b>n/a</b>	<b>-35%</b>	<b>-86%</b>	<b>340%</b>	<b>275%</b>	<b>31%</b>	<b>58%</b>	<b>35%</b>	<b>8%</b>	<b>7%</b>	<b>n/a</b>	<b>26%</b>	<b>10%</b>	<b>19%</b>	<b>25%</b>		<b>19%</b>	

[1] 2003-2006 incl. disco. operation; [2] Continuing Operations; [3] Excludes the land compensation from SHPL of US\$40.4 million at net income attributable to Chi-Med; [4] Excludes SHPL's R&D related subsidies of US\$2.5 million at net income attributable to Chi-Med for 2017 and H1 2017.

The logo consists of the letters 'CHI-' in white, sans-serif font, enclosed within a red rounded rectangle.

CHI-

The logo consists of the letters 'MED' in black, sans-serif font, enclosed within a white rounded rectangle with a black border.

MED

The text 'HUTCHISON CHINA MEDITECH' is written in a black, sans-serif font, centered horizontally across the middle of the image.

HUTCHISON CHINA MEDITECH

The text 'Thank you' is written in a black, sans-serif font, positioned in the lower right quadrant of the image.

Thank you