

# **Corporate Presentation**

January 2020 AIM/Nasdaq: HCM



# CHI-MED

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Use of Non-GAAP Financial Measures - This presentation includes certain 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.



# Agenda

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**Company Overview** 

# Building a global science-focused biopharma company from an established base in China...







#### **Global Innovation**

- 5 clinical drug candidates in US/EU development
- Building global clinical development footprint
- World-class ~500-person scientific team

# **China Oncology**



- Major market potential driven by regulatory reforms & high unmet medical need in oncology
- Elunate® (fruquintinib capsules) first ever homegrown cancer drug launched in China[1]
- 8 oncology assets in China development



### **Existing China Business**

- Cash generative China Commercial Platform
- Platform for future innovative drug launches



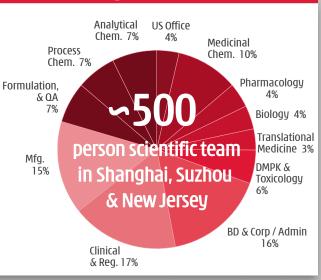
# Proven innovation & commercial operations

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9	Mr. CHRISTIAN HOGG, BSC, MBA Chief Executive Officer	P&G Procter & Gamble	31 / <b>20</b>
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9	Mr. ENRICO MAGNANELLI, BA, MBA Head of International Operations	<b>GILEAD</b>	21/2

#### Integrated Innovation Organization [1]







#### Commercial Team & Joint Ventures [1]

#### Commercial Team (subsidiaries):

- **~200** staff covering:
- Drug distribution & marketing operations; &
- New Oncology Business Dept.

#### 50/50 Joint Ventures:

- **~2,400** Rx medical sales reps.;
- **∽900** person OTC sales team; &
- >1,500 staff in two major factories

# Portfolio summary

# Multiple waves of innovation - progressing rapidly



# Dose Finding / Safety Run-In Fruquintinib + Tyvyt (PD-1) Solid Tumors [1]

Surufatinib + Tuoyi (PD-1)
Solid Tumors [1]

HMPL-523 (Syk) Indolent NHL

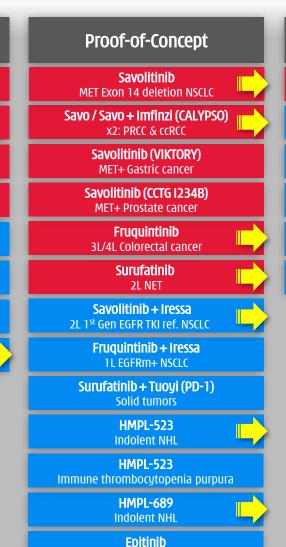
HMPL-689 (PI3Kδ) Indolent NHL

Fruquintinib + Tyvyt (PD-1)
Solid tumors

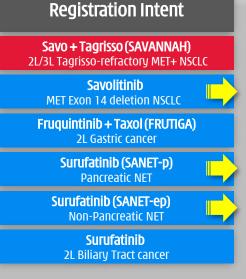
Fruquintinib + genolimzumab (PD-1)
Solid tumors

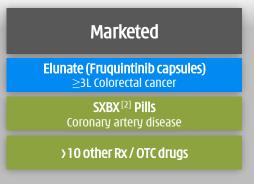
Surufatinib + Tyvyt (PD-1)
Solid tumors

HMPL-453 (FGFR1/2/3)
Solid tumors



Glioblastoma











2019 2020



Global **Innovation** 



China **Oncology** 

Data milestone/readout. = Development/commercial progress.

Savo + Imfinzi® Papillary RCC (CALYPSO) Ph. II Interim Data

Savo 2L gastric (VIKTORY) Ph. II Data

Savo + Tagrisso® **NSCLC (TATTON)** Ph. Ib Data (AACR)

**HMPL-689 (PI3Kδ) Indolent NHL** Ph. I Start (US/EU)

Savo

NSCLC Exon14del

Ph. II Data (AACR)

HMPL-523 (Syk) Indolent NHL Ph. I Start (US/EU)

Savo NSCLC Exon14del

Suru 2L Biliary tract Ph. II/III Start

Suru Non-P NET (SANET-ep) Ph. III Data (ESMO) **NDA Submission** 

Frua / Suru PD-1 combos

Frug + Taxol® 2L gastric (FRUTIGA) 1<sup>st</sup> Ph. III Interim

Frua 3L NSCLC (FALUCA) Ph. III Data (WCLC)

Frug NRDL Reimbursement

Savo + Imfinzi® Papillary RCC (CALYPSO) Ph. II Data Update

> Frug / Suru + PD-1 Initiation of U.S

Savo Papillary RCC (SAVOIŔ) Ph. III Early Data\*

development

Suru NET (US/EU) Ph. III Start\*\*

Savo + Tagrisso® Savo NSCLC, RCC, GC **NSCLC (SAVANNAH)** Anticipate further Ph. II Interim\* Ph. II/III studies

Fruq HMPL-523 (Syk) 3/4L colorectal (US/EU) Hem malignancies Ph. III Start\*\* Ph. I Exp Start\*\*\*

> HMPL-689 (PI3kδ) Hem malignancies Ph. I Exp Start\*\*\*

NSCLC Exon14del **Reg. Study Enrolled** NDA Submission\*:

> Suru P NET (SANET-p) Ph. III Interim

Frua / Suru PD-1 combos Savo

Suru + Tuoyi® (PD-1) Suru 2L Biliary tract Solid tumors Ph. I Data Ph. III Interim

Savo Savo + Iressa® NSCLC Exon14del 2L NSCLC Ph. II Data\* Ph. III Start

> Suru ED NET (SANET-ep) Launch

Frug + Taxol® 2L gastric (FRUTIGA) 2<sup>nd</sup> Ph. III Interim

HMPL-306 IDH 1/2 inhibitor Ph. I Start

HMPL-689 (PI3kδ) **Indolent NHL** Reg. Study Start\*\*\*

HMPL-523 (Svk) Indolent NHL Reg. Study Start\*\*\*

<sup>\*</sup> submission to scientific conference; \*\*subject to regulatory interaction; \*\*\* subject to supportive data; Targets: Savolitinib = MET; Fruquintinib = VEGFR1/2/3; Surufatinib = VEGFR1/2/3 / FGFR1 / CSF-1R; HMPL-523 = Syk;  $HMPL-689 = PI3K\delta$ : Indications; NHL = Non-Hodgkin's Lymphoma: NET = Neuroendocrine tumors; RCC = Renal cell carcinoma; NSCLC = Non-small cell lung cancer.





#### **Savolitinib** (c-MET)

Potential First-in-class small molecule selective MET inhibitor

Indications: MET-driven NSCLC; RCC; Gastric; Prostate cancer

Dosed to-date: [2] ~1,000 patients

NSCLC - Tagrisso® EGFR TKI refractory combinations:

Summary Data: Post 1<sup>st</sup>-gen TKI (n=105): ORR 64-67%
Post 3<sup>rd</sup>-gen TKI (n=69): ORR 30%

**PRCC** (n=44): ORR 18%; mPFS 6.2mo.

SAVANNAH global Ph. II/reg. underway<sup>[3]</sup>

Tagrisso® + savo

#### Fruquintinib (VEGFR1/2/3)

Potential Best-in-class small molecule selective VEGFR 1/2/3 inhibitor

Indications: Colorectal; NSCLC; Gastric cancer

Dosed to-date: ~1,650 patients in trials

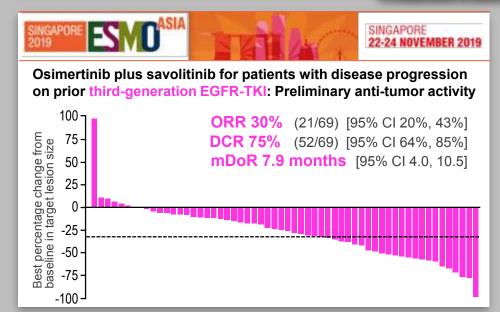
Launched in CRC Nov 2018 in China

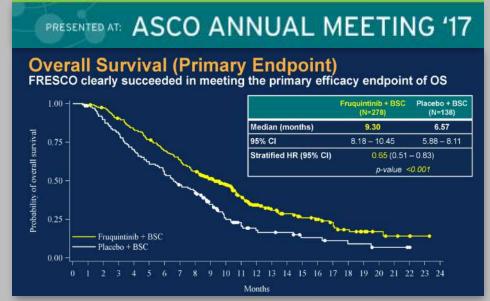
**3L CRC** (n=416): mOS 9.3mo. vs. 6.6mo. (SoC)

**3L NSCLC** (n=91): ORR 13%; mPFS 3.8mo. vs 1.1mo. (SoC)

**1L NSCLC (Iressa®combo)** (n=50): ORR 76% [1]

**2L Gastric (Taxol® combo)** (n=28): ORR 36%









#### **Surufatinib** (VEGFR, FGFR1, CSF-1R)

Unique small molecule VEGFR 1/2/3, FGFR1 & CSF-1R inhibitor

Dosed to-date: [1]

Indications: Neuroendocrine tumors (pNET/ep-NET);

~800 patients

Thyroid; Biliary Tract

Ep-NET China NDA
Filing Accepted

**Summary Data: Ep-NET** (n=198): ORR 10%; mPFS 9.2mo vs 3.8mo (Pbo)

**PhII interim pNET** (n=41): ORR 17%; mPFS 19.4mo.

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

Potential First-in-class small molecule selective Syk inhibitor

Indications: Indolent non-Hodgkin's lymphoma; AML; Immunol.

**Dosed to-date: >150 pts.** & ~118 healthy vol.

Dose escalation (5 cohorts) [2]

Summary Data: FL (n=10): ORR 30% CLL/SLL (n=3): ORR 33%

#### **HMPL-689** (PI3Kδ)

Potential Best-in-class small molecule selective PI3Kδ inhibitor

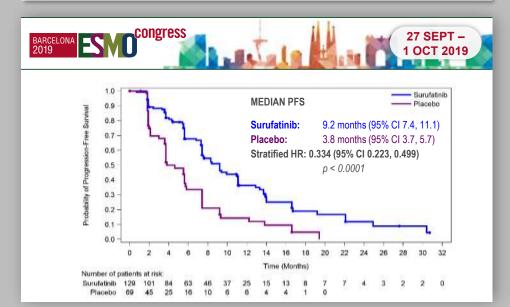
Indications: Indolent non-Hodgkin's

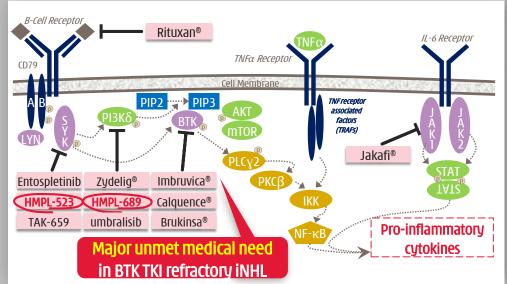
lymphoma

**Dosed to-date: ~40 pts.** & ~48 healthy vols.

Summary Data: Phase I dose escalation data

not yet published





[1] Dosed to-date = patients in all clinical trials (treatment & placebo); [2] American Society of Hematology. Blood, vol. 132 no. Suppl 1 5324 (Nov 2018); VEGFR = vascular endothelial growth factor receptor, FGFR1 = fibroblast growth factor receptor 1, CSF-1R = colony stimulating factor-1 receptor, Syk = spleen tyrosine kinase, PI3K\u00e8 = Phosphatidylinositol-3-Kinase delta, pNET = pancreatic neuroendocrine tumors, ep-NET = non-pancreatic neuroendocrine tumors, AML = acute myeloid leukemia, FL = follicular lymphoma, CLL = chronic lymphocytic leukemia, SLL = small lymphocytic leukemia.

# Superior safety allows for combinations TKI + TKI combos to address acquired resistance





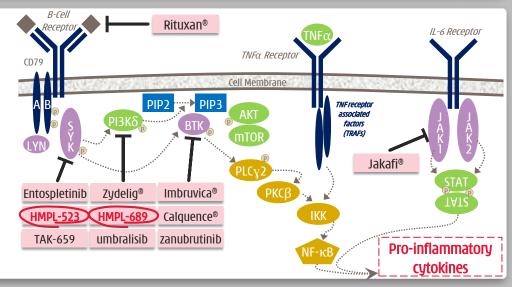
- MET amplification is the most common resistance mechanism for Tagrisso<sup>®</sup>.
- Requires addition of MET inhibitor savolitinib - in combo with Tagrisso<sup>®</sup>.

# RESULTS: CANDIDATE ACQUIRED RESISTANCE MECHANISMS WITH OSIMERTINIB (n=91)\* • No evidence of acquired EGFR T790M • The most common resistance mechanisms were MET amplification and EGFR C797S mutation • Other mechanisms included HER2 amplification, PIK3CA and RAS mutations Sec that y EGFR mutations: C797X: 7%: L7180-0797S: 1%: L7180-02079S: 1%: HER2 amplification: 2% HER2 mutation: 15% SPTBN: ALK: 1% BRAF mutations: (V600E): 3% KRAS mutations (V600E): 3% KRAS mutations (G12D)C, A146T): 3% MEX

CCND amps: 3%



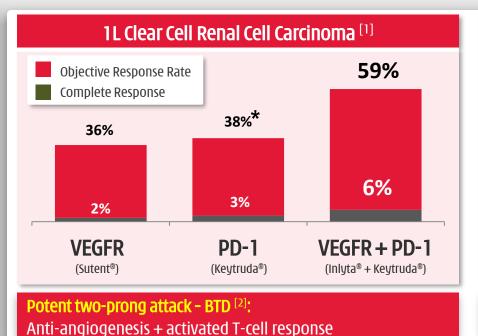
- C481S or PLCγ are the most common resistance mechanisms for Imbruvica®.
- Invalidating BTK inhibitor requires a possible Syk, PI3Kδ &/or BTK TKIs.



TKI = Tyrosine Kinase Inhibitor

# Immunotherapy combinations... assets potentially ideal TKI combo partners for immunotherapy

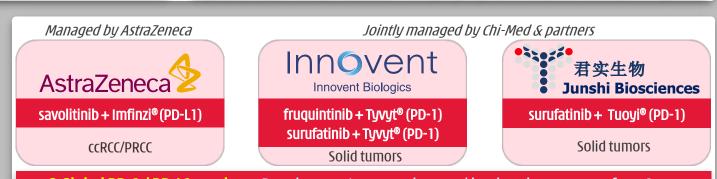




	Inlyta <sup>®</sup>	Fruquintinib	Surufatinib
Selectivity	Relatively selective	Highly selective	Selective angio-immuno kinase inhibitor
Status	Launched	Launched	Ph. IIIs ongoing
VEGFR1 (nM)	3	33	2
VEGFR2 (nM)	7	25	24
VEGFR3 (nM)	1	0.5	1
Phos-KDR (nM)	0.2	0.6	2
Other kinases (IC50 ← 100nM)	PDGFR $_{lpha}$ PDGFR $_{eta}$ c-Kit	none	CSF <u>-1R</u> FGFR1 FLT3 TrkB
Patent Expiration	2025/04/29 (US6534524B1)	2029 (without extension)	2030 (without extension)

**Fruq. uniquely selective** - unlike other TKIs with off-target toxicity **Suru. inhibits TAM production** - amplifying PD-1 induced immune response

Multiple global immunotherapy combo deals...



3 Global PD-1 / PD-L1 combos – Development now underway / in planning on savo, fruq & suru

# What is next from discovery?

### Differentiated assets against multiple targets

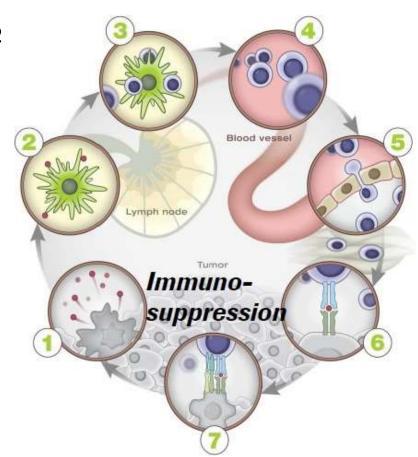


#### **Priming & activations**

- a0X40
- 4-1BB

#### Antigen release

- MET (savolitinib)
- EGFR (epitinib/theliatinib)
- Syk (HMPL-523)
- PI3Kδ (HMPL-689)
- FGFR (HMPL-453)
- IDH 1/2 (HMPL-306)
- ERK
- RIP1K



#### **Anti-angiogenesis**

- VEGFR (fruquintinib)
- VEGFR/FGFR (surufatinib)
- FGFR (HMPL-453)

#### **Negative regulators**

- Treg (HMPL-689)
- CSF-1R (surufatinib)
- IDOi
- AhRi
- TIM3
- TCBs
  - Pre-clinical small molecule
  - Pre-clinical antibody

Creating highest-quality range of assets against novel targets for use in combos



2a Savolitinib

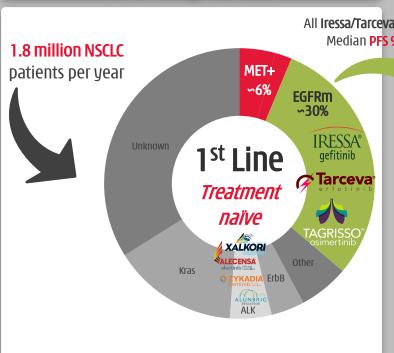
# Savolitinib

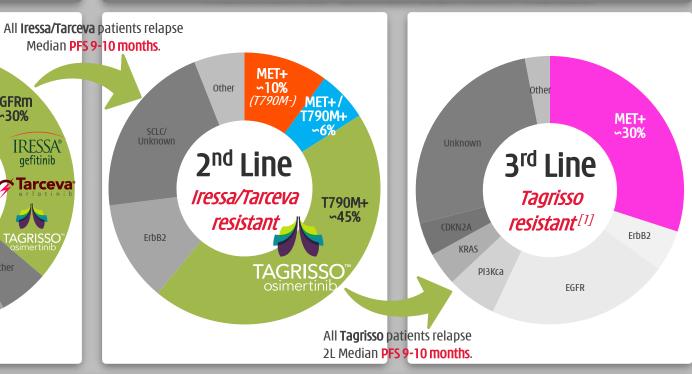
### Biggest opportunity is MET+ NSCLC



#### **Primary NSCLC**

#### Resistance-driven EGFRm+ NSCLC





	Target	Launch	2018 (\$m) <sup>[3]</sup>
Iressa	EGFRM	2003	\$518m
Tarceva	EGFRM	2004	550
Tagrisso	EGFRm / T790M	2015	1,860
Xalkori	ALK / ROS1 / MET	2011	524
Zykadia	ALK	2015	Not disc.
Alecensa	ALK	2015	650
Total Sales			→ 4.1b

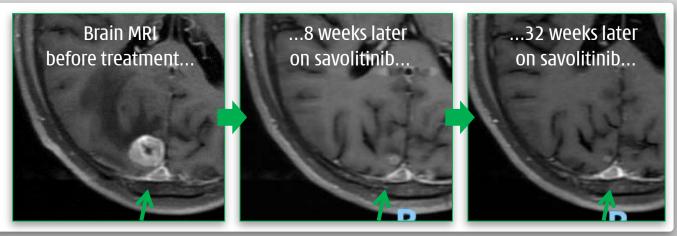
Launch	2016	2017	2018	9M 2019	
					Est. global sales
Dec-15	423	955	1,860	2,305 (+82%)	
					of ∽\$4-5 bn
					osimertinib <b>by 2022</b> <sup>[2]</sup> .

# Savolitinib - MET Exon 14 deletion NSCLC [1]

### Potential China NDA submission in 2020 [2]



- 4. Encouraging MET Exon14d NSCLC study China data at AACR 2019 [3]
- 41 pts; 31 pts efficacy evaluable.
- 💙 Promising antitumor activity.
- Rapid, durable tumor response observed.
- Anti-tumor activity observed in brain mets.
- Savolitinib generally well tolerated; most related 1 TEAEs were grade 1 or 2.



#### 5. MET Exon14d NSCLC potential NDA filing 2020 [2] 2019 2020 Mar 31, '19 -04'19 -**Potential NDA Topline results** Oral AACR Pres. submission • 41 patient data • CDE<sup>[4]</sup> discussion • Final results & potential Jun-Jul '19 - Phase II NDA submission registration study fully Incl. global safety data enrolled (n~60)

				P P
		Annual Incidence	Estimated mPFS	Pricing Reference
on-small Cell Lung Incer	100%	737,400		
MET Exon 14d NSCLC	2%	14,700	TBD	Tagrisso® China NRDL
IET gene ampl. SCLC	2-4%	14,700 - 29,000		
stric Cancer	100%	442,300	drive	orther MET- on patient
ET gene ampl.	4-10%	18,000 - 44,000		tions – savo otherapy

6. Savolitinib monotherapy China market opportunity

[1] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients; [2] We expect that the Phase II study of savolitinib in MET Exon 14d NSCLC would, if successful, be sufficient to support NDA submission; [3] Data cut-off Feb. 26, 2019. Lu S et al, CT031 - Preliminary efficacy and safety results of savolitinib treating patients with pulmonary sarcomatoid carcinoma (PSC) and other types of non-small cell lung cancer (NSCLC) harboring MET Exon 14 skipping mutations. Presented at American Association of Cancer Research Annual Meeting 2019, Atlanta, 6A, Mar. 31, 2019; [4] Center for Drug Evaluation of the National Medicinal Products Administration of China.

# Tagrisso® + savo in EGFR TKI refractory NSCLC TATTON B & D data - efficacy



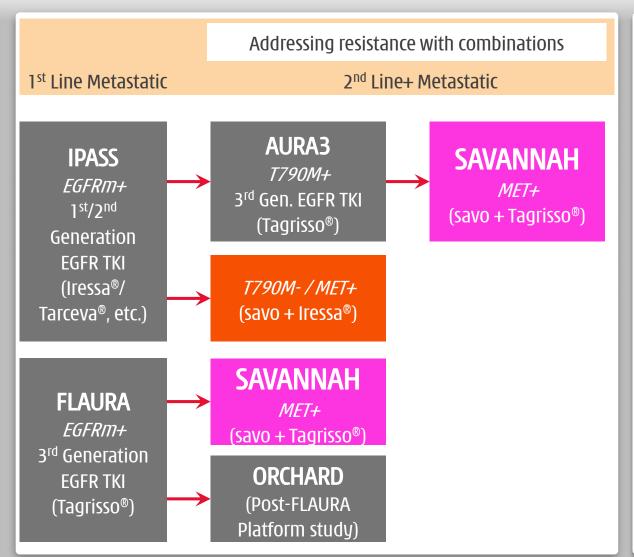
		TATTON Part D osimertinib 80 mg + savolitinib 300 mg		
	Part B1 (n=69) Prior third-generation EGFR-TKI	Part B2 (n=51)  No prior third-generation  EGFR-TKI  (T790M negative)	Part B3 (n=18)  No prior third-generation  EGFR-TKI  (T790M positive)	Part D (n=36)  No prior third-generation  EGFR-TKI  (T790M negative)
Objective response rate,* % [95% CI] Complete response, % Partial response, %	<b>30%</b> [20, 43] 0 30%	65% [5 <u>0, 78]</u> 0 65%	<b>67%</b> [41, 87] 0 67%	64% [46, 79] 0 64%
Non-response, % Stable disease (≥ 6 weeks) Progressive disease Not evaluable	45% 10% 14%	24% 6% 6%	33% 0 0	28% 3% 6%
Disease control rate, #% [95% CI]	<b>75%</b> [64, 85]	<b>88%</b> [76, 96]	<b>100%</b> [81, 100]	<b>92%</b> [78, 98]
Median DoR, months [95% CI]	<b>7.9</b> [4.0, 10.5]	<b>9.0</b> [6.1, 22.7]	<b>12.4</b> [2.8, NR]	<b>8.0</b> [4.5, NR]
Median PFS, months [95% CI]	<b>5.4</b> [4.1, 8.0]	9.0 [5.5, 11.9]	<b>11.0</b> [4.0, NR]	<b>9.1</b> [5.4, 12.9]

#### No reduction in efficacy with 300mg savo - SAVANNAH converted to 300mg dose

[1] Most patients were enrolled to Part B1, B2, B3 on 600 mg savolitinib, prior to weight-based dosing implementation, but following a protocol amendment in response to a safety signal of hypersensitivity, the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed ≤55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily; Best response data are for patients who had an opportunity to have two follow-up scans.; \*Complete or partial response confirmed at ≥4 weeks. \*Disease control rate = confirmed complete response + stable disease at ≥5 weeks.; CI, confidence interval; NR, not reached.

# Tagrisso® + savo in EGFR TKI refractory NSCLC SAVANNAH - global registration intent study





#### **SAVANNAH** (*NCT03778229*)

#### **S** Phase II single-arm study:

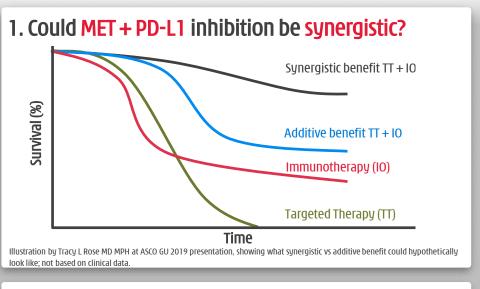
- Global N. & S. America, Eur., & Asia.
- Primary endpoint ORR.
- Secondary endpoints: PFS, OS, DoR & percent change in tumor size.
- Interim Analysis, potentially BTD enabling, mid 2020.
- Primary data completion est. 2021.

#### S ORCHARD study:

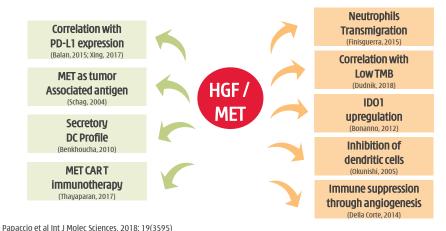
- Post FLAURA Platform study offering targeted treatments for all patients expect high enrollment.
- > MET+ patients prioritize to SAVANNAH.

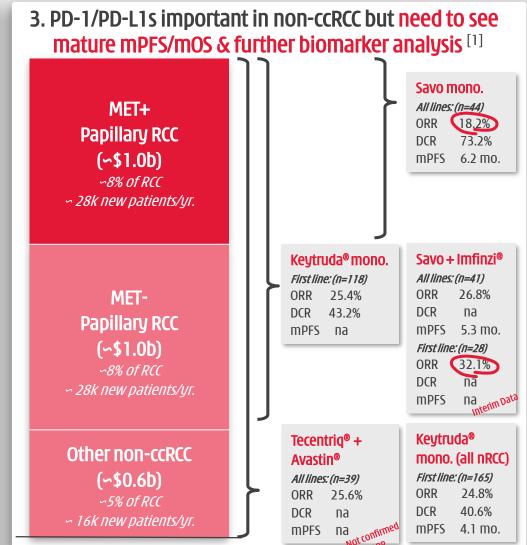
# Savolitinib in papillary RCC Important data planned at ASCO





#### 2. MET/HGF complex interplay with immune system.







#### Mechanism of Action

Anti-angiogenesis: cut off blood flow to tumor (VEGFR/FGFR).

Immunotherapy: inhibit expression of tumor-associated macrophages which cloak cancer cells from T-cell attack (CSF-1R).

Tumor-associated macrophages T-cells Angiogenesis



Surufatinib: angio-immuno kinase inhibitor

# Surufatinib

# Potentially our first un-partnered oncology drug launch

#### Two Phase III neuroendocrine tumor ("NET") registration studies...

- 25 China sites.
- 1° endpoint: median PFS.
- 2° endpoints: ORR, DCR, DOR, TTR, OS.



#### ...preparing for our first China launch...

04'19 -Sep 29, '19 - SANET-ep Jun 14. '19 - SANET-ed

2019

- **Interim Analysis**
- Study stopped early, a year ahead of schedule.
- Pre-NDA meeting with CDE.
- mPFS primary endpoint

Presentation at ESMO

- Tumor control secondary endpoints
- Placebo control

NDA Accepted

**Building out Oncology** 

**Full China** coverage

**Potential Late** 

2020 China launch

2020

# Surufatinib - China NET



Non-Pancreatic NET estimated to represent ∽80% of China NET

#### **Epidemiology -** *China NET & BTC patient populations*

Potential <u>First</u> suru			Annual Incidence	Estimated Prevalence	mPFS	NRDL Pricing References
monotherapy indication Non-	China NET	100%	67,600	<b>∽300,000</b> (Est. China ratio <sup>[1]</sup> )		
Two further	Non-Pancreatic NET	~80%	<b>∽54,100</b>	~240,000 (Est. China ratio <sup>[1]</sup> )	<b>9.2 mo.</b> (SANET-ep Ph.III)	Sutent® (∽US\$ 2,007/mo. <sup>[2]</sup> ) Afinitor®
surufatinib registration- intent studies	Pancreatic NET	~20%	<b>∽13,600</b>	<b>~30,000</b> (Est. China ratio <sup>[1]</sup> )	19.4 mo. (Ph.II) (SANET-p Ph.III TBD)	(∽US\$ 1,320/mo. <sup>[2]</sup> )
underway	Biliary Tract Cancer	100%	64,000		TBD	

NET is major unmet medical need in China – with long treatment duration

# G1/2 Advanced NET [1] (Ki-67 Index 0-20) Global opportunity in lung/other NETs & China wide-open



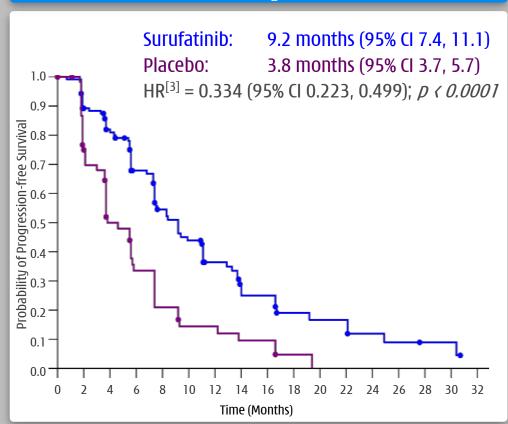
Site		est. %	Octreotide	Lanreotide	<sup>177</sup> Lu-Dotatate	Streptozocin	Sunitinib	Everolimus	Surufatinib
Disease status			Treatment naïve	Stable disease	Progressed in past 3 yrs.	Historical	Progressed in past 12 mo.	Progressed in past 6 mo.	Progressed in past 12 mo.
	Stomach	7%		CLARINET [2]	Historical Ph. II SSR over expression			RADIANT-4 [3]	SANET-ep
	Small bowel / appendix	9%	PROMID	CLARINET [2]	NETTER-1			RADIANT-4 [3]	SANET-ep
GI Tract	Colon & Rectum	31%		CLARINET [2]	Historical Ph. II SSR over expression			RADIANT-4 [3]	SANET-ep
Pancreas		6%		CLARINET [2]	Historical Ph. II SSR over expression	Historical	PHASE III	RADIANT-3 [3]	SANET-p Met primary endpt. (PFS)
Lung		20%						RADIANT-4 [3]	SANET-ep
Other	Other	~17%							SANET-ep
	Unknown Primary	~10%						RADIANT-4 [3]	SANET-ep

# G1/2 Advanced extra-pancreatic NET

Investigator assessed median PFS

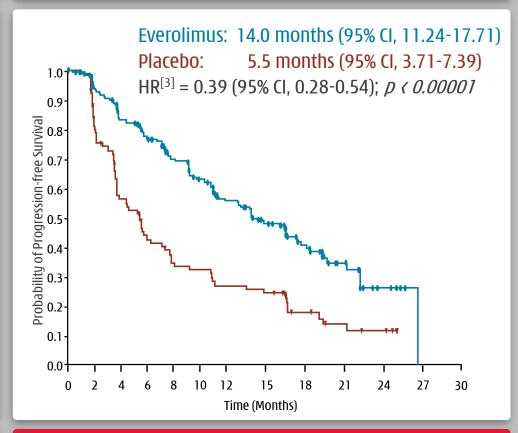


# **SANET-ep** [1] (n=198)



SANET-ep Primary (1°) endpoint was Investigator mPFS
BIIRC [4] mPFS for supportive analysis not 1° or 2°endpoint

# **RADIANT-4** [2] (n=302)



RADIANT-4 Primary (1°) endpoint was BIIRC [4] mPFS
Investigator mPFS not 1° or 2°endpoint

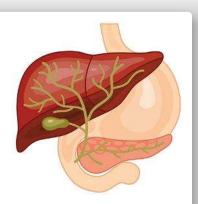
# Surufatinib

### Life cycle indications & other ongoing trials



#### Phase IIb/III study in 2L BTC

- First patient dosed in March 2019;
- Nearly all planned sites now activated;
- Interim analysis mid-2020, based on first 80 patients;
- Total enrollment ~300 patients.



#### PD-1 collaborations

- With Junshi (Tuoyi®): Dose expansion in multiple tumor types began YE2019;
- With Innovent (Tyvyt®): Global studies in planning.

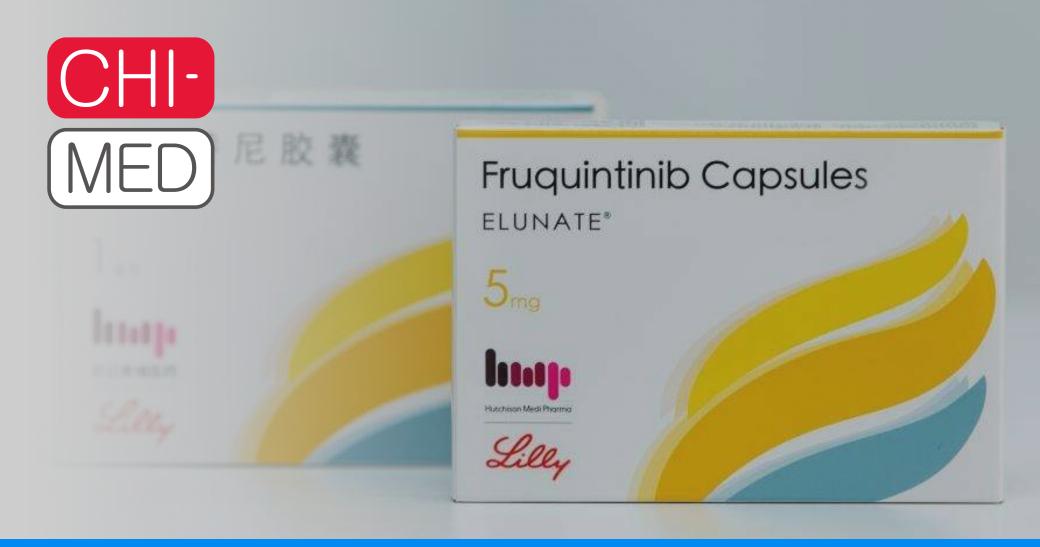




#### Ex-China development

- U.S. Phase Ib/II in P-NET & BTC initiated July 2018 NET enrollment complete;
- FDA End of Phase II meeting targeted for H1 2020;
- U.S. & Europe Phase III registration study expected to initiate in mid-2020.





**2c** 

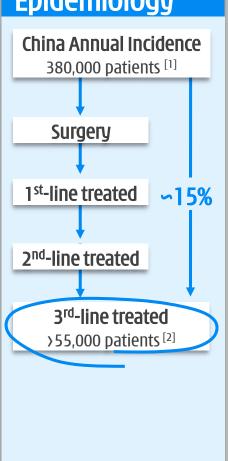
Elunate® (fruquintinib capsules)



# NRDL - highly competitive price



#### **Epidemiology**



#### Launch pricing [3]

#### Launch pricing (OOP [4])

~US\$ 3,260 per cycle (RMB 21,966 per cycle) (one cycle 4 weeks)

#### **Patient Access Program**

Cycle 1: ~US\$ 3,260

Cycle 2: ~US\$ 3.260

Cycle 3: Free (PAP<sup>[5]</sup>)

Cycle 4: Free (PAP<sup>[5]</sup>)

Cycle 5: ~US\$ 3,260

Cycle 6 onwards: Free (PAP<sup>[5]</sup>)

#### Total OOP cost to patients

~US\$ 9,800 (RMB 65,880)

#### Average Usage

∽Avq 5 mths / 5.5 cycles (to progression; 3.7 mo. mPFS [6] )

#### National Reimbursed Drug List (NRDL)

#### 2019 NRDL released by China's National Healthcare Security Administration ("NHSA")

- Announced Nov. 28, 2019; effective Jan. 1, 2020
- 8 newly listed oncology drugs, including Elunate®
- Reimburse 50-70% of patient costs under urban scheme

OOP costs for 3 per cycle <i>(all U</i>	BL CRC Patients JS\$) <sup>[7]</sup>	Urban Med. Insur. Scheme (UMI)	Non-UMI
Population % China		317m <i>23%</i>	1,053m <i>77%</i>
Elunate® (fruquintinib)	Pre-NRDL Post-NRDL	3,260 1,180	3,260 1,180
	3L CRC Pts OOP	350 - 600	1,1 <u>80</u>
Stivarga® (regorafenib)	Pre-NRDL Post-NRDL  3L CRC Pts OOP	4,490 2,450 <b>730 - 1.220</b>	4,490 2,450
	3L CKC PLS OUP	730 - <u>1.220</u>	2,450

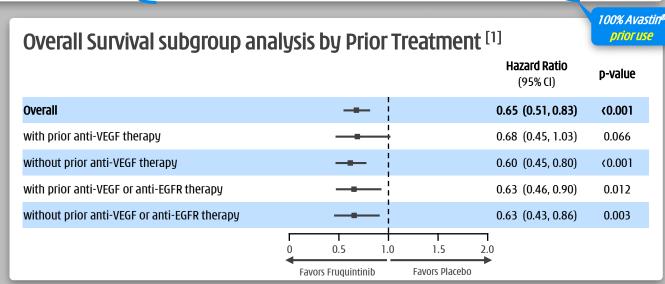


# Efficacy advantage



	FRESCO [1]  Mainland China		CONCUR  Chinese Patients (Mainland China, Hong Kong, Taiwan) [2]		CONCUR Mainland China, Hong Kong, Taiwan, Vietnam, South Korea		CORRECT	
Third-Line Metastatic Colorectal cancer								
Treatment arms	<b>Elunate</b> ®	Placebo	Stivarga®	Placebo	Stivarga®	Placebo	Stivarga <sup>®</sup>	Placebo
Patients (n)	278	138	112	60	136	68	505	255
Objective Response Rate, n (%)	4.7%	0.0%	3.6%	0.0%	4.4%	0.0%	1.0%	0.4%
Disease Control Rate, n (%)	62.2% +4	9.9 12.3%	45.5% +38	8.8 6.7%	51.5% +44	.1 7.4%	41.0% +2	6.1 14.9%
Median Progression-Free Survival (mPFS) (mo.)	3.7 +	.9 1.8	2.0 +0.	3 1.7	3.2 +1.	1.7	1.9 +	1.7
Median Overall Survival (mOS) (mo.)	9.3 +	2.7 6.6	8.4 +2.	2 6.2	8.8 +2.	6.3	6.4	5.0

- Advantage for Elunate® efficacy vs.
  Stivarga® in Chinese metastatic
  CRC patients;
- Advantage for Elunate® post VEGF/EGFR targeted therapy
  - mOS: 7.69 mo. vs. 5.98 mo. placebo (HR 0.63 & p-value 0.012)
  - mPFS: 3.65 mo. vs. 1.84 mo. placebo (HR 0.24 & p-value <0.001)





# Toxicity limitations of Stivarga®



	ELUNATE®	Stivarga <sup>®</sup>
BIOCHEMICAL ACTIVITY	IC <sub>so</sub> (nmol/L)	IC <sub>so</sub> (nmol/L)
On-Target Kinases:		
VEGFR1	33	13
VEGFR2	35	4.2
VEGFR3	0.5	46
Off-Target Kinases:		
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

#### Stivarga® liver toxicity black-box warning:

Increased liver function test monitoring (weekly if elevated) & remedial dose interruption.

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
- Monitor hepatic function prior to and during treatment. (5.1)
- 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)

	ELUNATE® Fruquintinib Capsules		Stivarga <sup>®</sup>	
3 <sup>rd</sup> -Line Metastatic Colorectal cancer	FRESCO Study Mainland China <sup>[1]</sup>		CONCUR Study (Mainland China, HK, Taiwan) <sup>[2]</sup>	
Treatment arms	<b>Elunate</b> ®	Placebo	Stivarga®	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%
VEGFR on-target related AES:				
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%
Off-target (i.e. non-VEGFR) related AEs:				
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%
Hepatic function (Liver function) AEs:				
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%
Tolerability:				
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%

### Elunate® superior safety - advantage especially for liver mets patients

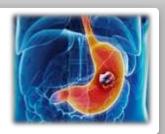


# Life cycle indications



#### Phase III in 2L gastric cancer (FRUTIGA)

- Second interim analysis by IDMC expected mid 2020;
- On track to complete enrollment H2 2020.



#### PD-1 collaborations

- With Innovent (Tyvyt®): dose/regimen finding ongoing;
- With Genor (genolimzumab): dose escalation ongoing;



#### Phase II in 1L NSCLC (in combination with Iressa®)

Study completed, keynote presentation of data at ESMO Asia in Nov 2019.



#### **Ex-China development**

- U.S. Phase Ib/II in CRC initiated in 2019 enrollment complete;
- FDA End of Phase II meeting targeted for H1 2020;
- U.S. & Europe Phase III registration study expected to initiate in mid-2020.





H1 2019 Financial Results, Cash & Guidance

# Cash position & 2019 Guidance

# \$384 million in available cash resources [1]



#### **Cash Position**

(at end June 2019)

- \$237 million cash / cash equiv. / Short term inv. [2]
- \$147 million additional unutilized banking facilities [3]
- \$64 million additional cash in JVs
- \$0 million in bank borrowings



(US\$ millions)	2019 Guidance
Research & Development Expenses	(130) - (170)
Adj. (non-GAAP) Group Net Cash Flows [4]	(90) - (120)

- Flexibility on future financing activity:
  - Sufficient capability to advance pipeline through multiple major value inflection points;
  - ➤ Non-dilutive finance from non-core CP divest. [5]



4 Summary

# 2020 Targets



### **Suru Launch**

- Chi-Med's first unpartnered oncology drug launch
- Oncology commercial team targeting ~300-350 reps

# Savo Breakout

- Submit 1<sup>st</sup> NDA (Exon14 NSCLC)
- SAVANNAH (w/Tagrisso®) interim



# **ELUNATE® NRDL**

- NRDL Jan 2020 broad China access
- **Stablish Elunate® as best-in-class VEGFR TKI**

# US & EU C&R Team

- S Fruq & Suru global Phase IIIs starting
- S HMPL-523 (Syk) & HMPL-689 (PI3Kδ) global development

**M&A** (In 2020 & beyond)

- Add large molecule development capability/assets
- Non-core commercial assets





HUTCHISON CHINA MEDITECH

Thank you



**A3** 

# **Appendix**

A1 Strategies

**Global Innovation** 

**China Oncology Opportunities** 

**Existing China Business** 

A2 Product Candidate Details

Further Corporate Information

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**Strategies - Global Innovation** 

Pushing the envelope on our most valuable assets

# One of China's largest & most established discovery platforms in oncology





## Global step-change innovation

• Aiming for multiple potential first-in-class assets



## Kinase selectivity - enable combos

• Limit off-target toxicity & address TKI resistance



Discovery of broad range of assets against novel targets





## Attack cancer from multiple angles at same time

#### **Immune Desert**

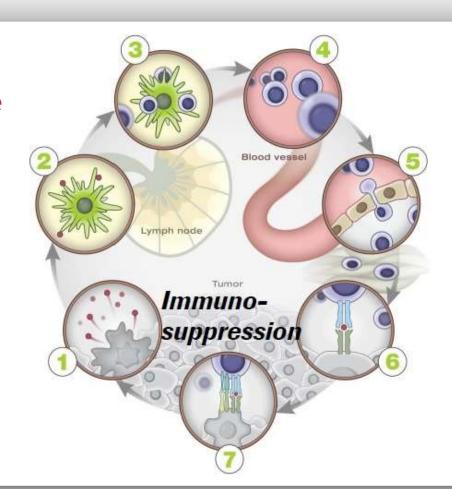
Insufficient T cell response

- Chemotherapies
- Vaccines
- CAR-T (pro-inflammatory strategies)
- TCB's

## Antigen Release

Aberrant genetic drivers

 Targeted therapies (small molecule & antibody)



#### **Excluded Infiltrate**

Inadequate T cell homing

- Anti-angiogenics
- Stromal targets
- Chemokines
- Vaccines

#### Inflamed

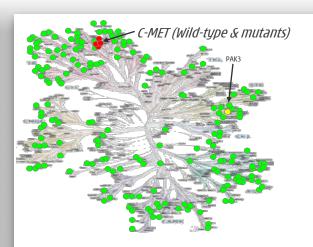
Inactivated T cell response

- Immunotherapies (address negative regulators)
- Vaccines

Need combinations of potent, yet tolerable drugs against specific targets

# Our advanced medicinal chemistry provides superior selectivity & safety profiles...



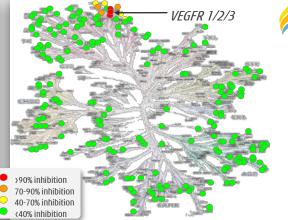


### Savolitinib

#### ~1,000 times

more selective to c-MET than next kinase (PAK3) [5]

Screening at 1µM against 253 Kinases





#### ∽250 times

more selective to VEGFR3 than next non-VEGFR kinase (Ret) [6]

	Discontinuations as % Enrolled			
Non-small cell lung cancer (NSCLC)	Due to AE	Withdrawn / Other	Total [1]	
Monotherapy - Tagrisso® / savolitinib				
Tagrisso® (osimertinib)	6%	6%	13%	
savolitinib 600mg QD PRCC (for reference only - not NSCLC) [2]	9%	5%	14%	
Combination - Tagrisso® + savolitinib				
savolitinib 600mg QD + Tagrisso® [3]	29%	6%	35%	
Approved treatments in NSCLC				
<b>Zykadia</b> ® (ceritinib)	10%	10%	20%	
Cyramza® (ramucirumab) + Taxotere®	15%	21%	37%	
<b>Keytruda</b> ® (pembrolizumab) 2mg/kg	10%	26%	37%	
<b>Opdivo</b> ® (nivolumab)	15%	4%	20%	
<b>Chemo doublet</b> (platinum + pemetrexed)	11%	17%	27%	
Taxotere® (docetaxel)	13%	22%	36%	

3 <sup>rd</sup> -Line Metastatic CRC		O Study nd China		JR Study K, Taiwan) <sup>[4]</sup>			
Treatment arms	Elunate®	Placebo	Stivarga®	Placebo			
VEGFR on-target related AEs:							
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%			
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%			
Off-target (i.e. non-VEGFR) related AEs:	Off-target (i.e. non-VEGFR) related AES:						
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%			
Hepatic function (Liver function) AEs:							
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%			
Tolerability:							
AE Leading to dose interruption	35.3%	10.2%	68.8%	25.0%			

## 5 assets in global development

### ...US/EU clinical & regulatory team fully operational



Program	Treatment	Indication	Target patient	Study name	Sites	Dose finding / safety run-in	Proof-of-concept	Registration
	<b>Savolitinib</b> + Tagrisso®	NSCLC	2L/3L EGFRm; Tagrisso® ref.; MET+	SAVANNAH	Global	Oxnard/Ahn – DF/SMC		
	<b>Savolitinib</b> + Tagrisso®	NSCLC	2L EGFRm; EGFR TKI ref.; MET+	TATTON	Global	Oxnard - Dana Farber		TATTON B/D Data
	Savolitinib + Imfinzi® (PD-L1)	Papillary RCC	All	CALYPSO	UK/Spain	Powles – Queen Mary's		ESMO Asia Nov 201
Savolitinib	<b>Savolitinib</b> + Imfinzi® (PD-L1)	Clear cell RCC	VEGFR TKI refractory	CALYPSO	UK/Spain	Powles – Queen Mary's		
MET	Savolitinib	Gastric cancer	MET+	VIKTORY	S Korea	Lee – Samsung Med. Ctr		Prelim. PoC at ASCO GU Feb 20
	<b>Savolitinib</b> + Taxotere®	Gastric cancer	MET+	VIKTORY	S Korea	Lee – Samsung Med. Ctr [1]		ASCO GO FED 20
	<b>Savolitinib</b> + Taxotere®	Gastric cancer	MET over-expression	VIKTORY	S Korea	Lee – Samsung Med. Ctr [1]		PoC published in
	Savolitinib	Prostate cancer	MET+	CCTG I234B	Canada	Kolinsky/Muk'jee/Ong/Chi		Can. Discovery Oct 20
ruquintinib	Fruquintinib	Colorectal cancer	3L/4L; Stivarga®/Lonsurf® ref./intol.		US	Eng /Desari - MD And. [2]		Planning US/EU regis
VEGFR 1/2/3	<b>Fruquintinib</b> + Tyvyt <sup>®</sup> (PD-1)	Solid tumors			US	In planning		<b>study</b> based on FRESC
Surufatinib	Surufatinib	Pancreatic NET	2L; Sutent®/Afinitor® refractory		US	Dasari/Yao – MD Anderson		US Ph. Ib  Planning US/EU regis
VEGFR 1/2/3; GFR1; CSF-1R	<b>Surufatinib</b> + Tuoyi <sup>®</sup> (PD-1)	Solid tumors				In planning		study based on
HMPL-523	HMPL-523	Indolent NHL			Australia			China Ph.III / US Ph.
Syk	HMPL-523	Indolent NHL			US	Fowler - MD Anderson		Global Ph.I/PoC data-
UMDI -690	HMPL-689	Healthy volunteers			Australia			now at n >150
<b>HMPL-689</b> PI3Kδ	HMPL-689	Indolent NHL			US	Ghosh/Cohen-Levine/Emory		Data-set now emerging in China Ph. I (n ~40)

[1] Further patient enrollment directed to savolitinib monotherapy arm due to the high efficacy observed; [2] in U.S., in E.U. Tabernero – Vall d'Hebron & Sobrero – Genova.

Note: MET = mesenchymal epithelial transition receptor, VEGFR = vascular endothelial growth factor receptor, EGFRm = epidermal growth factor receptor mutation, FGFR1 = fibroblast growth factor receptor 1, CSF-1R = colony stimulating factor-1 receptor, Syk = spleen tyrosine kinase, PI3Kδ = Phosphatidylinositol-3-Kinase delta, NSCLC = non-small cell lung cancer, RCC = renal cell carcinoma, NHL = Non-Hodgkin's Lymphoma, AACR = American Association of Cancer Research annual meeting, ASCO GU = American Society of Clinical Oncology Genitourinary Cancer Symposium, PoC = Proof of Concept.

### **Global Innovation**

### Main targets for 2020-2021





Aim for Savolitinib / Tagrisso® combo NDA submission



Savolitinib registration trial/s in papillary RCC



**Build out US/EU development operation** 

US/EU C&R operation set up in Florham Park, NJ





Accelerate development of 4 un-partnered global assets

- Fruq (ex-China) & suru registration studies & exploration of combos with PD-1s;
- Syk & PI3K\u03b8 registration studies & exploration of combos with other TKIs



Aim to continue to move novel drug candidates into global development each year





Strategies - China Oncology

Next-gen oncology drugs to meet major needs in China



## China oncology - ~24% of world's cancer patients<sup>[1]</sup> [MED]



## Industry's attention turning to unmet medical need in China oncology

- Regulatory reforms in China addressing low SoC [2]
- Major investment inflow



## Chi-Med is a first mover

- Elunate® launch in 3L mCRC; First ever in China [3]
- Deep pipeline 8 clinical drug candidates with 5 registration studies underway/set to start in China



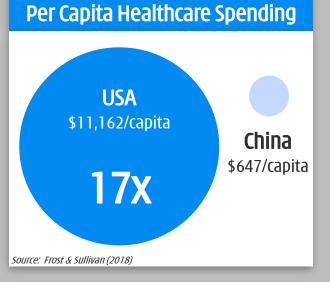
## **Major commercial opportunity**

National Drug Reimbursement; Medical coverage

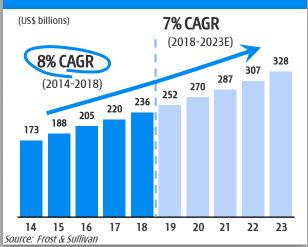


# China now world's 2<sup>nd</sup> largest pharma market ...investment, approvals & access all accelerating rapidly

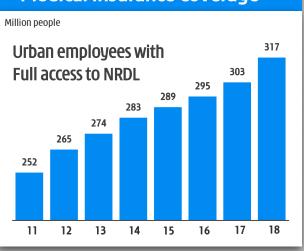




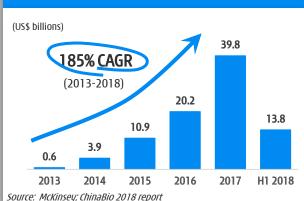




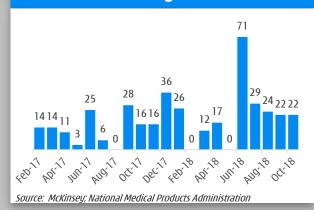
#### Medical Insurance Coverage [1]



#### PRC Healthcare VC/PE Funds [2]



#### Number of Priority Review NDAs [3]



#### **Improved Access since 2017**

- 128 western drugs added to NRDL;
- Further 17 oncology drugs added to NRDL in Oct 2018 (15 in Jul 2017);
- Essential drug list expanded from 520 to 685 molecules. Including oncology.

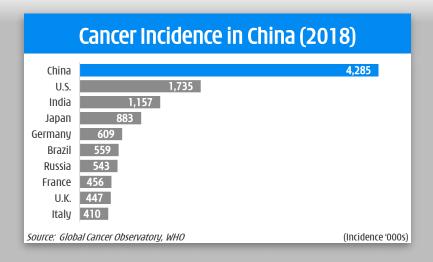
Source: McKinsey

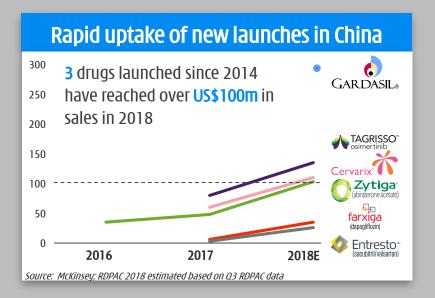
<sup>[1]</sup> Urban Basic Medical Care Insurance (for both employees & residents) - total persons covered at year-end. National Bureau of Statistics (2017); includes rural residents from 2017 and beyond; [2] Funds raised; [3] NDA = New Drug Application. Note: CAGR = Compound annual growth rate.

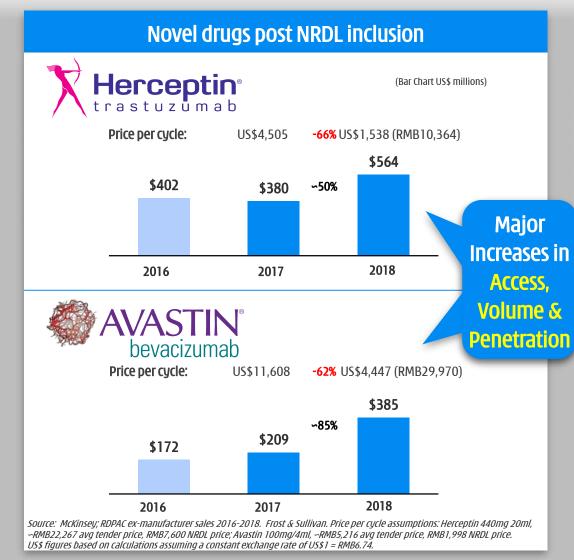
## Cancer is a major unmet need in China



...investments in launches/access starting to have an impact







## 8 assets in China development

## CHI-

## ...fruq launched – savo/suru NDAs & Syk/PI3K $\delta$ PoC ahead

Program	Treatment	Indication	Target patient	Study name	Sites	Dose find / safety run-in	Proof-of-concept	Registration	Fully Enrolled
Cavalitinih	Savolitinib	NSCLC	MET Exon 14 deletion		China	Lu Shun – SH Chest Hosp.			NDA H1'20
<b>Savolitinib</b> MET	<b>Savolitinib</b> + Iressa <sup>®</sup>	NSCLC	2L EGFRm; Iressa® ref.; MET+		China	Wu Yilong – GD General			
	Savolitinib	Gastric cancer	MET+		China	Shen Lin – BJ Univ. Tumor			Launched
	Fruquintinib	Colorectal cancer	≥3L; chemotherapy refractory	FRESCO	China	Li Jin - Fudan Univ.			Nov 2018
	Fruquintinib + Taxol®	Gastric cancer	2L	FRUTIGA	China	Xu Ruihua - Sun Yat Sen			Interim OK
Fruquintinib	Fruquintinib	NSCLC	3L; chemotherapy refractory	FALUCA	China	Lu Shun – SH Chest Hosp.			April 2019
	<b>Fruquintinib</b> + Iressa®	NSCLC	1L EGFRM		China	Lu Shun – SH Chest Hosp.			ESMO Asia
	<b>Fruquintinib</b> + Tyvyt® (PD-1)	Solid tumors			China	Bai Yuxian - Harbin Med. U.			Nov 2019
	<b>Fruquintinib</b> + genolimzumab (PD-1)	Solid tumors			China	Li Jin – Fudan Univ.			Met Primary
	Surufatinib	Pancreatic NET	All	SANET-p	China	Xu Jianming - #5 Med. Ctr.			Endpt (PFS)
Surufatinib	Surufatinib	Non-Pancreatic NET	All	SANET-ep	China	Xu Jianming – #5 Med. Ctr.			Jan 2020
VEGFR 1/2/3; FGFR1; CSF-1R	Surufatinib	Biliary tract cancer	2L; chemotherapy refractory		China	Xu Jianming – #5 Med. Ctr.			NDA accepted
·	<b>Surufatinib</b> + Tuoyi <sup>®</sup> (PD-1)	Solid tumors			China	Shen Lin - BJ Univ. Tmr.			Nov 2019
HMPL-523	HMPL-523	B-cell malignancies	All		China	Multiple leads by sub-types		Planning	China Ph.II/III
Syk	HMPL-523	ITP	All		China	Yang – CN Hem. Hosp.			al iNHL types
HMPL-689	HMPL-689	Indolent NHL			China	Cao/Zhou - Fudan/Tongji		Ph. Ib da	ta now n >150
РІЗКδ								Data-se	t emerging in
Epitinib	Epitinib	NSCLC	EGFRm with brain metastasis		China	Wu Yilong – GD General		China	Ph. I (n ∽40)
EGFR	Epitinib	Glioblastoma	EGFR gene amplified		China	Ying Mao – SH Huashan			
Theliatinib	Theliatinib	Esophageal cancer	EGFR over-expression		China	Shen Lin – BJ Univ. Tumor [1]			
EGFR wt									
HMPL-453	HMPL-453	Solid tumors			China	Xu Ruihua - SYS			
FGFR 1/2/3									

## China Oncology

### Main targets for 2020-2021





## Establish Elunate® as the best-in-class VEGFR TKI in China market

- Work with Lilly to maximize penetration & sales performance;
- Aggressively expand PD-1 combination collaborations & broader LCI program
- 3

### Launch our un-partnered oncology drugs

- Surufatinib NDAs in all neuroendocrine tumors (pancreatic & non-pancreatic);
- Expand Oncology Commercial Organization in China
- 3

## Savolitinib NDA in MET Exon 14 NSCLC

3

### Progress development pipeline

- Syk & PI3K\darkdot into registration studies & aim to establish PoC for epitinib, theliatinib & FGFR;
- Aim for further novel drug candidates into early development each year





Strategies – Existing China Business

Cash generation & China commercial know-how / infrastructure







# Chi-Med's Commercial Platform in China Integrated platform built from ground up



2 National House-Hold Name Brands



Major Commercial & Production Scale

people in over 330 [1] cities & towns in China.

Drugs in >25,200 hospitals detailing ~82,000 doctors.

Sold **~4.8** billion doses of medicine in 2018.

Leadership Market Sha<u>res</u>

Market leader in the subcategories/markets in which we compete [2]:

Banlangen:<sup>[5]</sup> ~54%

OTC Anti-viral /flu TCM

Rx Cardiovascular TCM

OTC Angina TCM

JVs with 3 Major China Pharmas











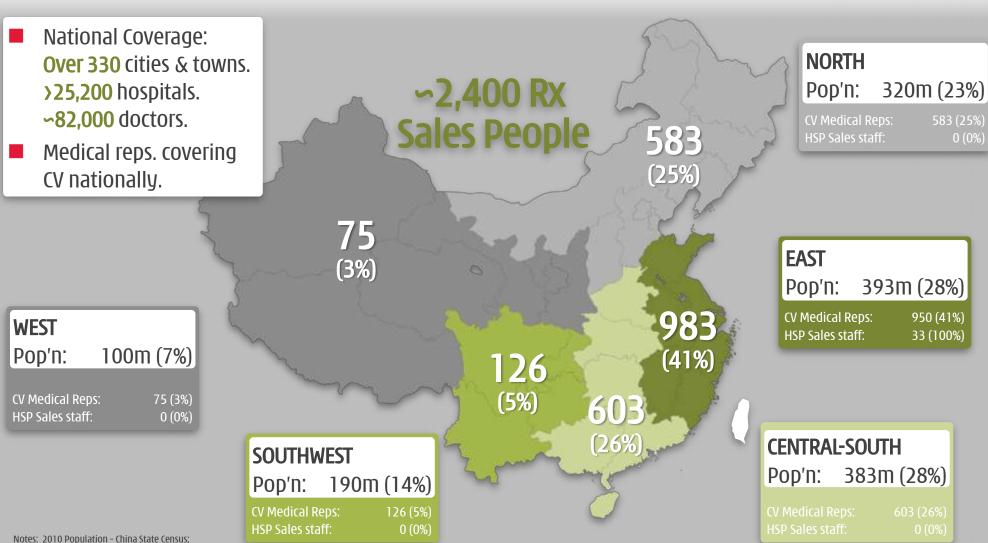






# Established Rx Commercial Platform in Mainland China... Chi-Med management run all day-to-day operations

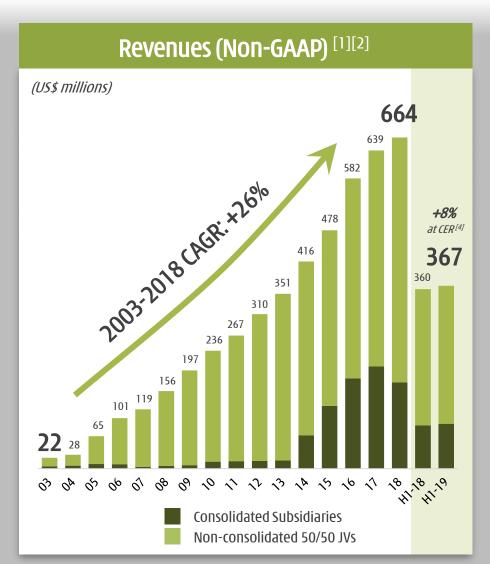


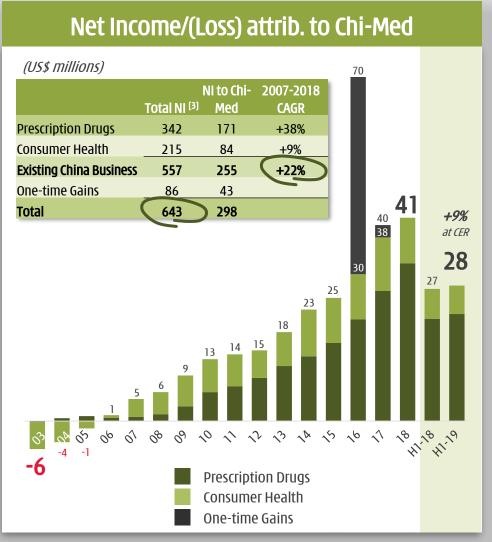


CV = Cardiovascular Chi-Med Rx sales team data = September 30, 2019

# Chi-Med's Commercial Platform in China Proven track record, ~\$300 million in net income since inception







## Existing China Business

#### Plans for 2020-2021



- **Continue organic growth** 
  - Focus on proprietary prescription drug products
- Build out synergies with China Oncology Organization
- Strategically evaluate potential for M&A
- Focus on cash generation





 A1d

**Recent Operating Highlights** 

## H1 2019 Financial results R&D expense accelerated to \$74.5m in first 6 months







	2018	H1-18	H1-19	Growth	at CER [2] (Non-GAAP)
GROUP REVENUES  Unconsolidated JV Revenues	<b>214.1</b> <i>491.5</i>	102.2 271.7	102.2 276.9	<b>-</b> +2%	<b>+5%</b> +8%
SEGMENT NET INCOME/(LOSS) [1]					
INNOVATION PLATFORM	(102.4)	(52.9)	(63.8)	-21%	-29%
COMMERCIAL PLATFORM	41.4	26.9	27.7	+3%	+9%
Prescription Drugs Business Consumer Health Business	32.1 9.3	20.8 6.1	21.8 5.9	+5% -4%	+11% +2%
Chi-Med Group Costs	(13.8)	(6.7)	(9.3)	-39%	-39%
GROUP NET LOSS [1]	(74.8)	(32.7)	(45.4)	-39%	-48%
EPS Attrib. to Ord. S-H (Basic) (US\$)	(0.11)	(0.05)	(0.07)		





#### Savolitinib



- Reached enrollment goal on Phase II registration study MET Exon 14 deletion NSCLC;
- AstraZeneca collaboration leading global position in EGFR-TKI resistant NSCLC;
- **Emerging signal for savolitinib/Imfinzi**® (PD-L1) combo renal cell carcinoma.

#### **Surufatinib**



- Positive China Phase III and NDA accepted with Priority Review for non-pancreatic NET un-blinded a year ahead of schedule; Positive China Phase III for pancreatic NET;
- Initiated Phase IIb/III biliary tract cancer; & Phase II for PD-1 combos.

#### Elunate® (fruquintinib capsules)

- Inclusion on NRDL from 1 Jan 2020 for 3L colorectal cancer in China;
- Cleared Phase III interim analysis 2L gastric cancer (FRUTIGA);
- Initiated Phase I for PD-1 combos.





## Other Recent Operating Highlights

#### B-cell malignancies / non-Hodgkin's lymphoma

- HMPL-523 (Syk) >150 patients dosed in China/Australia Phase I/Ib; to guide registration strategy in late 2019;
- HMPL-689 (PI3K $\delta$ ) Phase II dose selected in China & expansion underway;
- **US/EU Phase I 1st patient dosed** for both HMPL-523 & HMPL-689.

#### **Organization**

- Accelerating expansion of New Jersey-based international C&R operations;
- Establishing China oncology commercial team > 100 commercial staff in place, focused on medical affairs & preparation for potential surufatinib launch.

#### Discovery

IND submission on HMPL-306 – an isocitrate dehydrogenase (IDH) 1/2 inhibitor.





## **Product Candidate Details**

Further details on each drug candidate





Savolitinib (AZD6094)

Potential first-in-class selective MET inhibitor

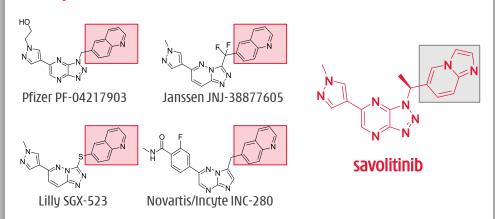
## Savolitinib (AZD6094)





#### Potential first-in-class selective MET inhibitor

- 1. Strong potential to become first selective MET inhibitor approved in certain indications.
  - ✓ 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) & biomarker testing.
- 3. Savolitinib design eliminates renal toxicity first generation of selective MET inhibitors encountered ~900 patients involved in clinical studies to date.



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

#### 2. MET is aberrant in many tumor settings. [7]

		New Cases (2018)			
Indication	Amplification	Mutation	Over- Expression	Global	China
Gastric	10%	1%	41%	1,033,700	442,300
Non-small Cell Lung Cancer	4%/16%/30% [1]	2% [2]	39%	1,779,800	737,400
Head & Neck	17-39%	11% [3]	46% [4]	887,700	137,000
Colorectal	10%	3%	65%	1,801,000	426,700
Papillary Renal Cell Carcinoma	64%	70-100% [5]	55%	45,400	3,700
Clear Cell Renal Cell Carcinoma	54%	NA	35%	281,300	57,500
Esophagus	8%	NA	92%	572,000	271,600
Prostate	NA	NA	54/83% [6]	1,276,100	99,300

#### 4. AstraZeneca collaboration & 2016 amendment.

- \$20m received upfront (Dec 2011);
- \$120m in development/approvals milestones (\$25m received as of June 2019);
- 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%);
- From 9% up to 18% tiered royalty ex-China [8] & 30% flat rate China royalty on all product revenues.

## Savolitinib - MET Exon 14 deletion NSCLC

#### China's lead MET inhibitor

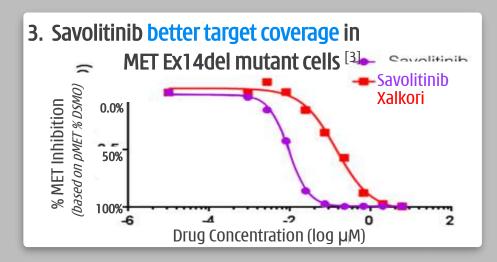


1. Competitive landscape outside China:

			Treatment Line	N	BICR [1] ORR	95% CI
Capmatinib	coloctivo MET	ASCO 2019 #9004	2/ <u>3L</u>	69	<b>40.6%</b> (28/69)	28.9%, 53.1%
(Novartis/Incyte)	selective MET	ASCO 2019 #9004	1L)	28	<b>67.9%</b> (19/28)	47.6%, 84.1%
<b>Tepotinib</b> (Merck Serono)	selective MET	ASCO 2019 #9005	39% 1L, 61%≥2L	51	<b>45.1%</b> (23/51)	31.1%, 59.7%
Xalkori <sup>®</sup>	multi kinasa	WCLC 2018 #13453	38% 1L	65	<b>32.3%</b> (21/65) <sup>[2]</sup>	21%, 45% <sup>[2]</sup>
(Pfizer)	multi-kinase	WCLC 2018 #12937	Median 1L (1L-4L)	25	<b>40.0%</b> (10/25)	21%, 61%

## 2. Xalkori® a multi-kinase TKI – selective MET inhibitors reporting better response – superior selectivity.

	Savolitinib IC <sub>50</sub>	Xalkori® IC <sub>50</sub>	Savolitinib vs. Xalkori®
EBC1 Viability	2nM	19nM	10x
EBC1 pMET	1	39	40x
293T MET (wild type)	7	79	11x
293T MET (Ex14del)	9	140	16x

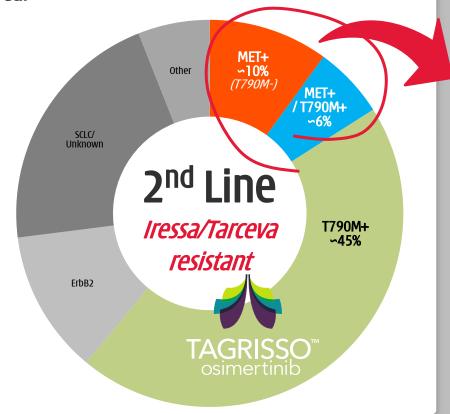


## Savolitinib - EGFR-TKI resistant NSCLC



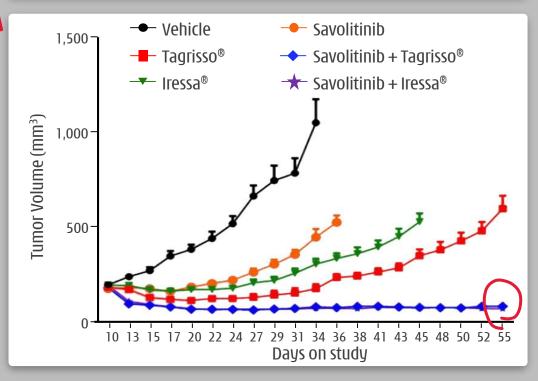
### Very strong preclinical rationale for combination w/ EGFR-TKIs

1. 2<sup>nd</sup> Line NSCLC is a **fast and 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.



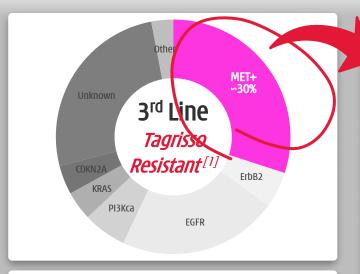
## Savolitinib - 2L/3L NSCLC<sup>[1]</sup> - TAGRISSO<sup>™</sup> resistant





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





3 out of 3 MET+ patients responded to savo/Tagrisso® combo.





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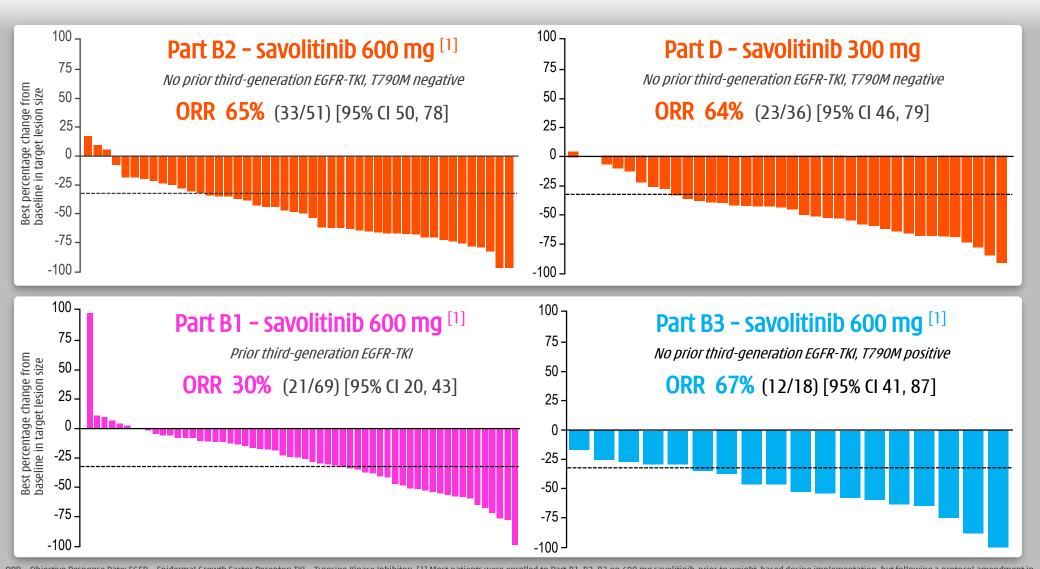
Pt	EGFR mutation	# Prior Therapies	Prior 3 <sup>rd</sup> gen TKI	TISSUE (NGS, FISH)	PLASMA CTDNA (NGS)
1	L858R	1		<i>MET</i> amp, T790 WT	<i>MET</i> amp, T790M ND
2	Del19	1		-	T790M ND
3	Del19	2	Υ	-	T790M ND
4	L858R (de novo T790M)	2	Υ	<i>MET</i> amp, <i>EGFR</i> amp T790M (germline)	-
5	L858R	3	Υ	T790wt,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

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

### TATTON B & D data - ORR

## Tagrisso® + savolitinib in EGFR TKI refractory NSCLC

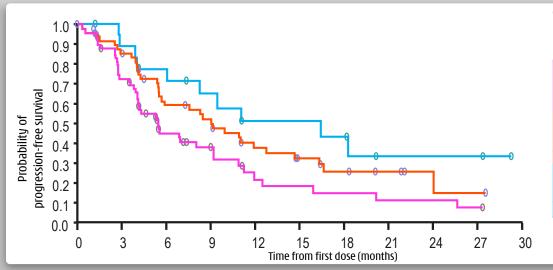




### TATTON B & D data - PFS

## Tagrisso® + savolitinib in EGFR TKI refractory NSCLC

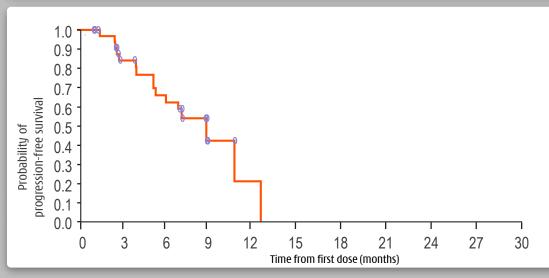




<b>5.4</b> [4.1, 8.0]	
<b>3.4</b> [4.1, 0.0]	<b>2.6</b> [0.0-27.3]
<b>9.0</b> [5.5, 11.9]	<b>10.1</b> [0.0-27.5]
<b>11.0</b> [4.0, NR]	<b>14.7</b> [1.2-29.3]
	<b>9.0</b> [5.5, 11.9]

#### Progression data had a maturity of 62%.

Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment. Circles indicate censored observations.



	Median PFS, months [95% Cl]	Median (range) duration of follow-up in censored patients, months
Part D  No prior third-generation EGFR-TKI,  T790M negative; (300 mg; n=42)	<b>9.1</b> [5.4, 12.9]	<b>3.0</b> [0.0-11.0]

#### Progression data had a maturity of 40%.

Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment. Circles indicate censored observations.

# Tagrisso® + savo in EGFR TKI refractory NSCLC TATTON B & D data - AEs & tolerability



Event, n (%)	All Part B (n=138) osimertinib 80 mg + savolitinib 600 mg <sup>[1]</sup>	Part D (n=42) osimertinib 80 mg + savolitinib 300 mg [1]
Any AE	135 (98)	39 (93)
Any AE possibly related to savolitinib	115 (83)	25 (60)
AE grade ≥3	79 (57)	16 (38)
AE possibly causally related to study treatment leading to discontinuation of:		
Savolitinib	38 (28)	9 (21)
Osimertinib	14 (10)	2 (5)
Any AE leading to death	6 (4)	2 (5)
Any SAE	62 (45)	11 (26)

[1] Most patients were enrolled to Part B1, B2, B3 on 600 mg savolitinib, prior to weight-based dosing implementation, but following a protocol amendment in response to a safety signal of hypersensitivity, the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed  $\leq$ 55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily. Part D data are preliminary, therefore, for osimertinib, the mean actual treatment exposure was 8.5 months vs 6.1 months for Parts B and D, respectively, and 7.1 months vs 4.9 months for savolitinib, for Parts B and D, respectively; Han J. et al, "TATTON expansion cohorts: a Phase Ib study of osimertinib plus savolitinib in patients with EGFR-mutant, MET-amplified NSCLC following disease progression on a prior EGFR-TKI", #LBA, ESMO Asia, Singapore, November 23, 2019;

## TATTON B & D data - AES & SAES Most common AEs<sup>[1]</sup> independent of causality & SAEs (≥3%)<sup>[2]</sup>



AF* p (0/)	All Part B	s (n=138)	Part D	(n=42)
AE*, n (%)	All grades	Grade ≥3	All grades	Grade ≥3
Nausea	67 (49%)	4 (3%)	13 (31%)	0
Fatigue	48 (35)	6 (4)	4 (10)	0
Decreased appetite	47 (34)	5 (4)	6 (14)	1 (2)
Vomiting	46 (33)	6 (4)	5 (12)	0
Oedema peripheral	44 (32)	3 (2)	8 (19)	0
Diarrhoea	39 (28)	4 (3)	8 (19)	2 (5)
Paronychia	30 (22)	3 (2)	7 (17)	0
Pyrexia	29 (21)	1 (1)	6 (14)	0

AF* p (0/)	All Part B	(n=138)	Part D	(n=42)
AE*, n (%)	All grades	es Grade≥3 All gra		Grade ≥3
Rash	26 (19%)	3 (2%)	8 (19%)	0
Stomatitis	26 (19)	0	4 (10)	0
Constipation	26 (19)	0	3 (7)	0
Pruritus	24 (17)	1 (1)	5 (12)	0
Headache	23 (17)	0	3 (7)	0
Myalgia	22 (16)	3 (2)	6 (14)	1 (2)
Cough	22 (16)	0	4 (10)	1 (2)
AST increased	21 (15)	9 (7)	2 (5)	0
Pneumonia	15 (11)	7 (5)	7 (17)	5 (12)

SAE**, n (%)	All Part B (n=138)	Part D (n=42)
Pneumonia	5 (4%)	4 (10%)
Anaphylactic reaction	6 (4)	1 (2)
Pneumothorax	6 (4)	1 (2)
Pyrexia#	5 (4)	0
Dyspnoea	5 (4)	0
Drug hypersensitivity	4 (3)	1 (2)
Diarrhoea	4 (3)	1 (2)
Back pain	4 (3)	0
Pulmonary embolism	3 (2)	2 (5)

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





## Encouraging in MET+ / T790M-, next step under discussion

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

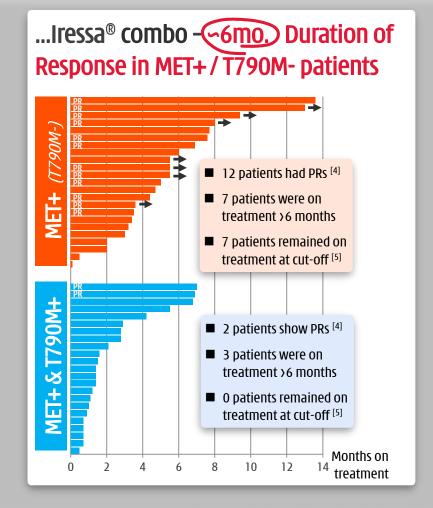
WCLC 2017	MET+ / T790M+ (n = 23)	MET+ <i>(T790M-)</i> (n = 23)	MET+/T790M unk. (n = 5)
Confirmed response	2 (9%)	12 (52%)	2 (40%)
Stable disease ≥ 6 weeks	9 (39%)	7 (30%)	2 (40%)
Progressive disease / death	7 (30%)	3 (13%)	0
Not Evaluable	5 (22%)	1 (4%)	1 (20%)
MET status all centrally confirmed.			1

-

MET status locally or centrally confirmed.

#### ...vs. TATTON B data (savo / Tagrisso® combo) [3]

	MET+/T790M+ (n = 11) WCLC 2017 <sup>[2]</sup>	MET+ <i>(T790M-)</i> (n = 46) AACR 2019 <sup>[3]</sup>
Confirmed response	6 (55%)	24 (52%)
Stable disease≥ 6 weeks	NA (43% central confirm.)	16 (35%)
Progressive disease / death	NA (0 central confirm.)	3 (7%)
Not Evaluable	NA (0 central confirm.)	3 (7%)



[1] EGFRm NSCLC; [2] WCLC 2017 - Yang J-J, et al. A Ph.lb Trial of savolitinib plus gefitinib for patients with EGFR-mutant MET-amplified advanced NSCLC; [3] AACR 2019 - Sequist, et al. A Ph.lb Trial of savolitinib plus gefitinib for patients with EGFR-mutant MET-amplified NSCLC after progression on prior epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI); [4] PR = Partial Response; [5] Aug 21, 2017.

## Safety & tolerability

## Tagrisso® & savo both highly selective/tolerable monotherapies

			L	Efficacy		Discontinuations as % Enrolled		
US FDA Approval	Treatment	Disease setting	n	ORR	Median PFS (mo.)	Due to AE	Withdrawn / Other	Total [5]
Monot	therapy - Tagrisso®/ savolitini	b						
30-Mar-17	Tagrisso® (osimertinib)	<b>2L</b> EGFRi-refractory T790M+ NSCLC (AURA3)	279	71%	10.1	6%	6%	13%
	savolitinib 600mg QD monotherapy [3]	All-lines Papillary RCC FOR REFERENCE ONLY NOT NSCLC	109 [1]	18%	6.2	9%	5%	14%
Combi	nation - Tagrisso® + savolitini	b						
	savolitinib 600mg QD + Iressa® (gefitinib) [2]	≥ <b>2L</b> EGFRm+ MET+ T790M- NSCLC after 1st-gen EGFR TKI (expansion)	51	52%	ND	20%	14%	33%
	savolitinib 600mg QD + Tagrisso® [3][4]	≥ <b>3L</b> EGFRm+ MET+ NSCLC after 3 <sup>rd</sup> -gen EGFR TKI <b>(TATTON B1)</b>	69	30%	5.4		ND	ND
	savolitinib 600mg QD + Tagrisso® [3][4]	≥2L EGFRm+ MET+ T790M- NSCLC after 1st-gen EGFR TKI (TATTON B2)	51	65%	9.0	28%	ND	ND
	savolitinib 600mg QD + Tagrisso® [3][4]	≥ <b>2L</b> EGFRm+ MET+ T790M+ NSCLC after 1st-gen EGFR TKI <b>(TATTON B3)</b>	18	67%	11.0		ND	ND
	savolitinib 300mg QD + Tagrisso® [3]	≥ <b>2L</b> EGFRm+ MET+ T790M- NSCLC after 1st-gen EGFR TKI <b>(TATTON D)</b>	36	64%	9.1	21%	ND	ND
Approv	ed treatments in NSCLC							
12-Dec-14	<b>Cyramza</b> ® (ramucirumab) + <b>Taxotere</b> ®	<b>2L</b> NSCLC after plat-chemo	624	23%	4.5	15%	21%	37%
24-0ct-16	<b>Keytruda</b> ® (pembrolizumab) 2mg/kg	<b>2L</b> PD-L1+ (TPS≥1%) NSCLC after plat-chemo (KEYNOTE-010)	345	18%	3.9	10%	26%	37%
2-0ct-15	<b>Keytruda</b> ® (pembrolizumab) 10mg/kg	<b>2L</b> PD-L1+ (TPS≥1%) NSCLC after plat-chemo (KEYNOTE-010)	346	18%	4.0	9%	27%	36%
9-0ct-15	<b>Opdivo</b> ® (nivolumab)	<b>2L</b> NSCLC after plat-chemo	292	19%	2.3	15%	4%	20%
4-Mar-15	<b>Opdivo</b> ® (nivolumab)	<b>2L</b> squ. NSCLC after plat-chemo	135	20%	3.5	12%	8%	20%
2008	<b>Chemo doublet</b> (platinum + pemetrexed)	2L NSCLC (AURA3)	136	31%	4.4	11%	17%	27%

[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] WCLC 2017 #8995; [3] ESMO Asia 2019 LBA#2; [4] Most patients were enrolled to 600mg savolitinib, prior to weight-based dosing implementation, but the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed ≤55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily; [5] Total discontinuations = Discontinuations NOT due to Disease Progression or Death; ND = Not Disclosed.

Tagrisso® + savo combo tolerable even in late-stage ≥3L patients

# PRCC - unmet medical need Lower response rates to treatments



#### 1. Limited treatment options for non-ccRCC

### Several approved therapies in ccRCC [3]

Immunotherapy setting new treatment paradigm

FIRST LINE – clear-cell RCC [4]	ORR	mpfs	mos
Placebo (avg. multiple studies)	∽2%	<b>∽3.5</b>	∽15.0
Torisel® (mTOR)	8.6%	5.5	10.9
<b>VEGFR, multi-kinase small molecule</b> (multiple compounds)	12-31%	6-11	21-28
<b>Opdivo® + Yervoy®</b> (PD-1/CTLA-4 immunotherapy) <sup>[5]</sup>	42%	∽11.6	NR
<b>Keytruda® + Inlyta®</b> (PD-1/VEGFR combo)	59.3%	15.1	NR
Bavencio® + Inlyta® (PD-L1/VEGFR combo)	51.4%	13.8	NR
SECOND LINE – clear-cell RCC			
Placebo (avg. multiple studies)	∽0%	<b>∽2.0</b>	∽14.0
<b>Cabometyx®</b> (VEGFR/MET, multi-kinase SM) <i>(METEOR)</i>	17%	7.4	21.4
Inlyta® (VEGFR, multi-kinase SM)	23%	8.3	20.1
<b>Lenvima® + Afinitor®</b> (VEGFR, multi-kinase SM + mTOR)	35%	14.6	25.5
<b>Opdivo®</b> (PD-1 mAb) <i>(CheckMate025)</i>	25%	4.6	25.0

## **NO CATEGORY 1 recommendation**

FIRST LINE – non clear-cell RCC <sup>[4]</sup>	ORR	mPFS m	OS
<b>Sutent®</b> (VEGFR, multi-kinase SM) <sup>[4]</sup>	9%	6.1	6.2
<b>Afinitor®</b> (mTOR) [4]	3%	6.1 4.1	4.9
SECOND LINE – non-clear-cell RCC <sup>[4]</sup>			
<b>Sutent®</b> (VEGFR, multi-kinase SM) <sup>[4]</sup>	10%	1.8 r	ıa
<b>Afinitor®</b> (mTOR) [4]	9%	2. <u>8</u> r	na

2. RCC est. ∽\$13.0 bn. market by 2030 [1] Clear-cell RCC (~\$10.4b) ∽80% of RCC ∽ 290k new patients/yr. [2] Non-Clear-cell RCC

#### 3. Unmet medical need:

MET+
Papillary RCC
(~\$1.0b)

∽8% of RCC ∽ 28k new patients/yr.<sup>[2]</sup>

METPapillary RCC
(~\$1.0b)

∽8% of RCC ∽ 28k new patients/yr.<sup>[2]</sup>

Other non-ccRCC (~\$0.6b)

∽5% of RCC ∽ 16k new patients/yr.<sup>[2]</sup>

(**\$2.6b**)

\$\times 20\% of RCC

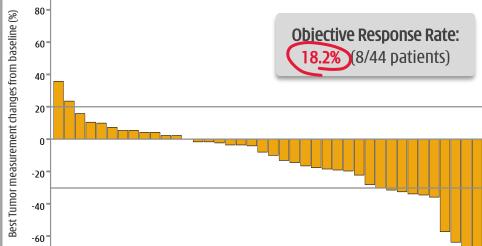
\$\times 73k new patients/yr.^{[2]}

[1] Frost & Sullivan; [2] Frost & Sullivan, based on US incidence mix and global incidence rate in 2018; [3] NCCN Guideline for kidney cancer (Version 1.2020, June 7, 2019) preferred or category 1 options, RCC = renal cell carcinoma; [4] ORR = Objective Response Rate, mPFS = median Progression-Free Survival, mOS = median Overall Survival, NR = not reached; For approved subgroup of patients; [5] only approved for patients with intermediate or poor risk RCC.

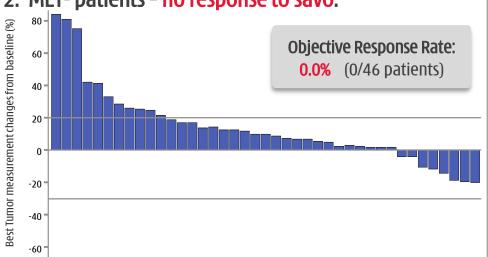
# Savolitinib - PRCC Phase II Clear efficacy & durable response in MET+ PRCC patients







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



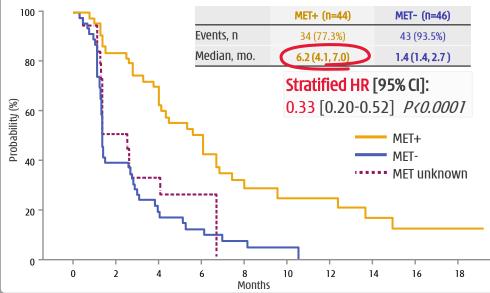
## 3. Disease Control Rate ("DCR") - big advantage in MET+ with DCR 73.2% vs. MET- 28.2%.^

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%)

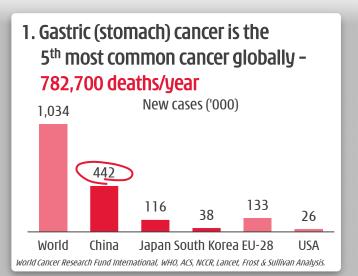
<sup>\*</sup> P=0.002 versus MET-independent subgroup (Fisher exact test). Responses assessed according to RECIST version 1.1.† Unconfirmed responses excluded. ^ Evaluable patients.

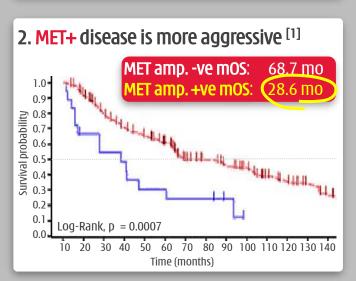
#### 4. Median PFS - big advantage in MET+ patients.

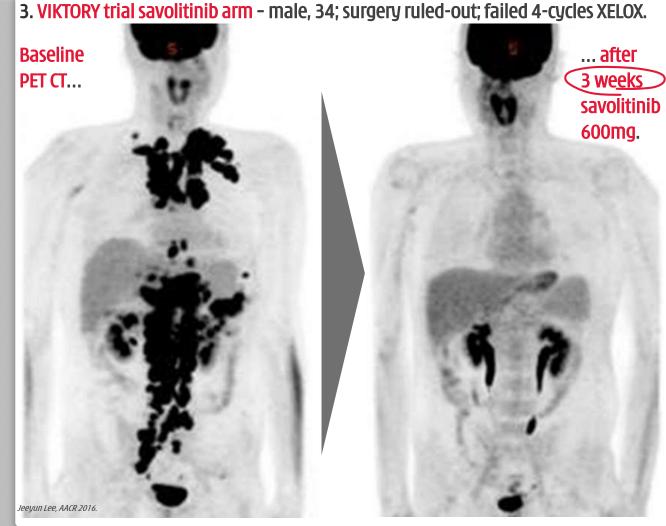


# Savolitinib - MET+ gastric cancer A major problem in east Asia - Japan, South Korea & China



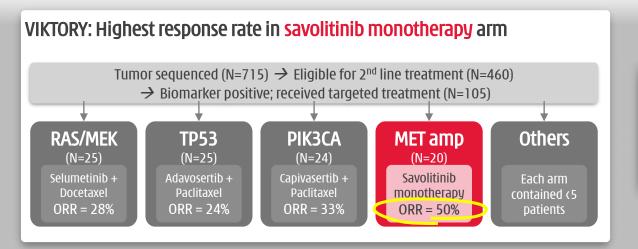


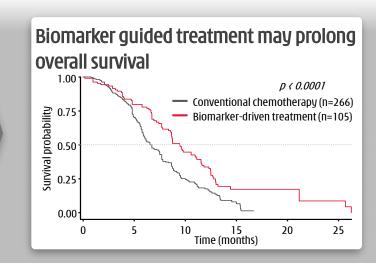


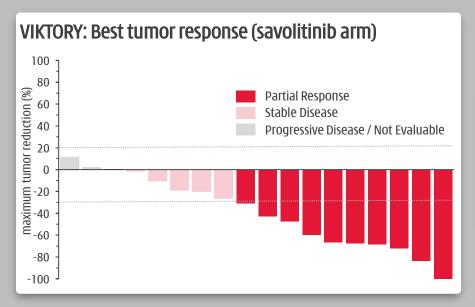


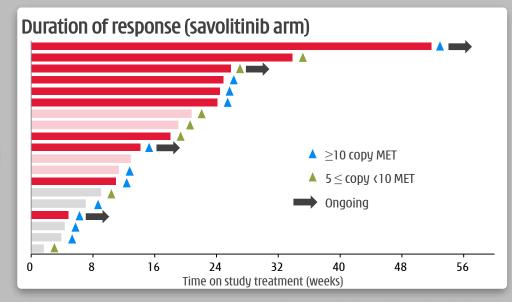
# Savo potential in gastric cancer VIKTORY Phase II trial highly promising in MET+ gastric cancer















Elunate® (fruquintinib capsules)

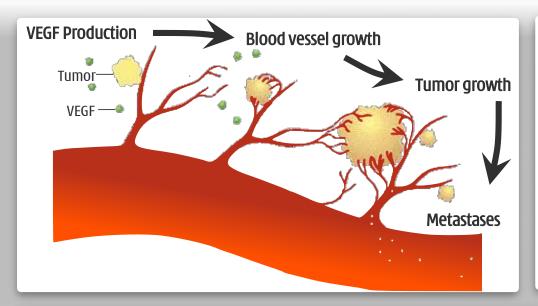
Highly selective anti-angiogenesis inhibitor

## Fruquintinib - 24hr full target coverage

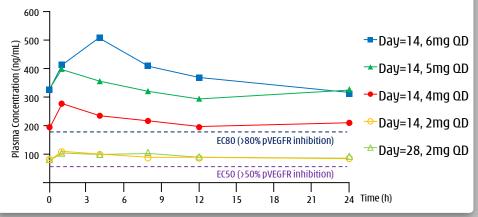




The most selective VEGFR inhibitor in clinical trials globally [1]





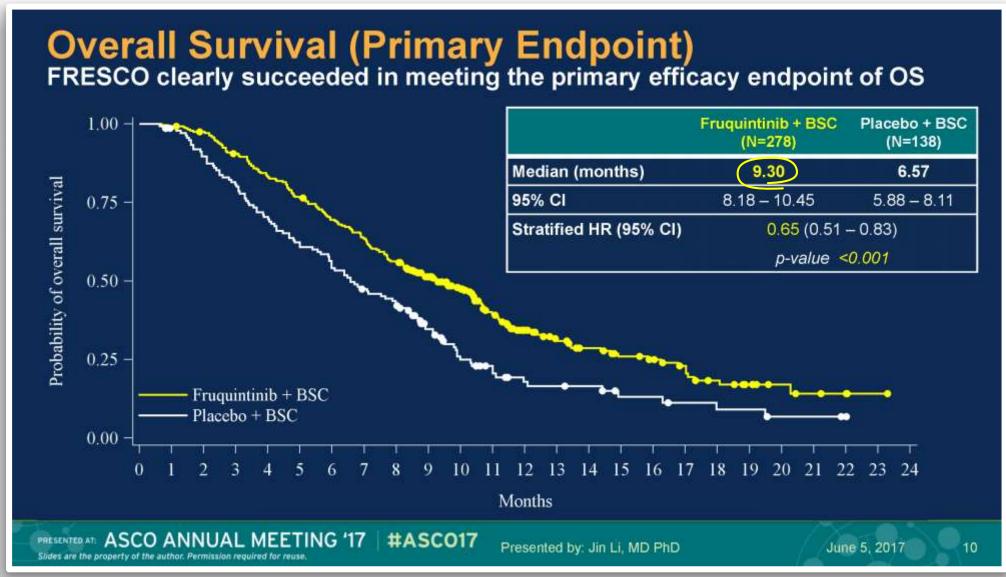


#### 2. Selectivity and potency superior to competitors' drugs.

	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	$\begin{array}{c} \text{VEGFR1,2,3, BRK, PDGFR}\alpha, \\ \text{PDGFR}\beta, \text{c-Kit, Tie2, EphB2} \end{array}$	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 <u>~6,000</u> (D28)
Efficacy in Phase I	22 patients PR: 4 (18%), DCR: 27%	45 patients <sup>[2]</sup> 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%

# Fruquintinib – 3L/4L colorectal cancer Develop in US/EU for rego/TAS-102 ref./intol. patients<sup>[1]</sup>







ment.

National Institutes for Food

and Drug Control (NIFDC)

Shanghai Food and Drug

Administration (SHFDA)

## Many "Firsts" for China biotech

Center for Food and Drug

Inspection (CFDI)

Critical Path





Center for Drug

Evaluation (CDE)



## Launched - Nov. 25, 2018



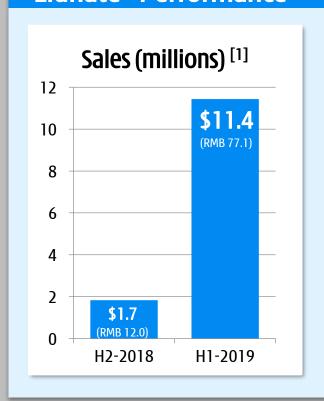


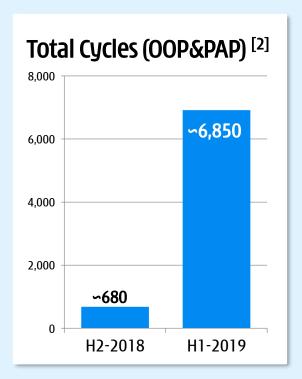


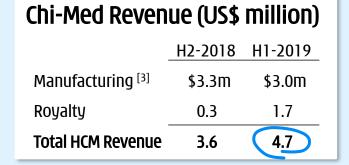
## H1 2019 performance



#### Elunate® Performance









### Elunate® early progress - PAP working but NRDL will provide greater access

[1] Royalties to Chi-Med in H2 2018 and H1 2019 of \$0.261m and \$1.715m, respectively; at the lowest tier royalty rate of 15%, this implies net sales from third parties to Lilly of \$1.7m and \$11.4m, respectively; at RMB:US\$ exchange rate of 6.87:1 and 6.74:1, respectively, this implies RMB sales of 12m and 77m, respectively; [2] Treatment cycle = 28 day, i.e. assume three x 7 capsule 5mg packs per cycle or five x 21 capsule 1mg packs per cycle; 00P = 0ut of pocket payment; PAP = Patient access program; [3] Sales of Elunate manufactured by Chi-Med to Eli Lilly.



## Fruquintinib Capsules China VEGFR landscape



### Competitive landscape - small molecule VEGFR TKIS

Brand STIVARGA®	Indication/s 3L CRC /2L GIST		Sales (US\$ million) [1]	2011	2012	2013	2014	2015	2016	2017	2018 21	Q1-2019 20
<i>(regorafenib)</i> Bayer AG	2L HCC	Mar 2018	List Price (US\$/mo.)							4,368	NRDL Oct-18	2,352
NEXAVAR®	Unres. RCC & HCC		Sales (US\$ million) [1]	80	96	96	93	91	97	108	130	50
<i>(sorafenib)</i> Bayer AG	Diff. Thyroid can.		List Price (US\$/mo.)						7,250	NRDL Jul-17	3,610	3,610
SUTENT®	RCC, GIST, pNET	2007	Sales (US\$ million) [1]	9	33	41	21	26	29	27	24	7
<i>(sunitinib)</i> Pfizer			List Price (US\$/mo.) [4]							5,544	NRDL Oct-18	2,498
INLYTA®	2L adv. RCC	2015	Sales (US\$ million) [1]					3	12	16	13	5
<i>(axitinib)</i> Pfizer			List Price (US\$/mo.)							5,957	NRDL Oct-18	1,787
VOTRIENT®	RCC	2017	Sales (US\$ million) [1]							5	12	5
<i>(pazopanib)</i> Novartis			List Price (US\$/mo.)							7,891	NRDL Oct-18	2,348
AITAN®	3L Gastric can.	Dec 2014	Sales (US\$ million) [2]					<b>∽4</b> 5	∽126	219	258	~82
<i>(apatinib)</i> Hengrui			List Price (US\$/mo.)						2,870	NRDL Jul-17	1,810	1,810
FOCUSV®	3L NSCLC	June 2018	Sales (US\$ million) [3]								∽190	~83
<i>(anlotinib)</i> Sino Biopharn	n		List Price (US\$/mo.)								NRDL Oct-18	981

Elunate® first 6 mo. sales progressing... relative to all MNC VEGFRi China launch sales [5]

## FALUCA - Third-line NSCLC Monotherapy Presented at WCLC 2019



## FALUCA Phase III (enrolled Dec. 2015 to Feb. 2018)

- Met all secondary endpoints: mPFS; ORR; DCR; & DoR [1];
- Did not achieve primary endpoint of median OS, however:
  - Anti-tumor therapies after disease progression reduced OS diff.
  - Higher percentage of placebo pts received subsequent treatments.

## Significant difference in subsequent anti-tumor treatments (ATT)

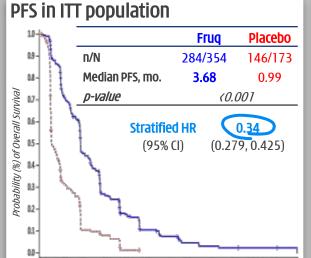
- **Chemotherapy:** Fruq. 29.7% vs. Placebo 53.8%
- Targeted therapies (VEGFi and/or EGFRi): Fruq. 20.9% vs. Placebo 31.2%
- Tagrisso® & aniotinib just approved in 2017

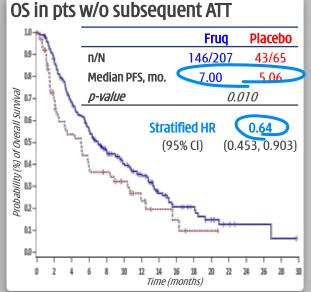
#### Efficacy Endpoints (Intent-to-Treat) [2]

	Fruq. (N=354)	Placebo (N=173)	p-value
mOS (mths)	8.94	10.38	0.841
mPFS (mths)	3.68	0.99	(0.001
ORR	13.8% (49)	0.6% (1)	(0.001
DCR	<b>66.7%</b> (236)	24.9% (43)	(0.001

### Good safety; most Grade ≥3 TEAEs target-related & clinically manageable.

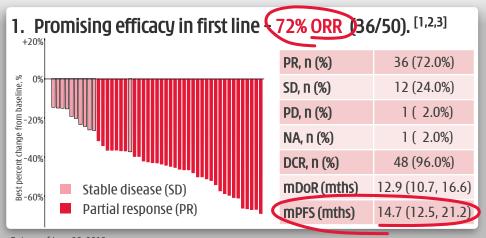
Patient (%)	Frug (N=354)	Pbo (N=173)				
TEAE ≥ Grade 3	216 (61.2%)	47 (27.6%)				
Leading to discontinuation	37 (10.5%)	9 (5.3%)				
Leading to interruption	61 (17.3%)	7 (4.1%)				
Leading to dose reduction	85 (24.1%)	2 (1.2%)				
Hypertension	74 (21.0%)	5 (2.9%)				
Hand-foot syndrome	39 (11.0%)	0				





# Fruquintinib – 1L NSCLC combo w/ IRESSA® gefitinib Two small molecule TKIs allow for better management of tox.

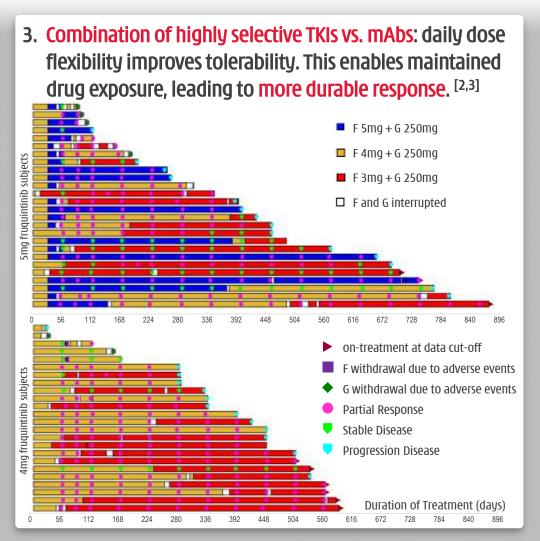




Data as of June 28, 2019.

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

Adverse Events ("AEs")	Iressa® or Tarceva® FLAURA <sup>[5]</sup> N = 277, n (%)	Avastin® + Tarceva® [6] N = 75, n (%)	5mg Fruq. + Iressa® N = 26, n (%) <sup>[3]</sup>	4mg Fruq. + Iressa® N = 24, n (%) <sup>[3]</sup>
All AEs, any grade	273 (98%)	≥74 (≥99%)	26 (100%)	24 (100%)
All AEs, Grade ≥3	124 (45%)	68 (91%)	17 (65%)	11 (46%)
AEs leading to death	6 (2%)	0 (0%)	3 (12%)	0 (0%)
AEs to VEGFRi disc.	NA	31 (41%)	6 (23%)	4 (16%)
Grade ≥3 AEs:				
Liver function	33 (12%)	6 (8%)	13 (50%)	3 (13%)
Hypertension	NA	45 (60%)	1 (4%)	1 (4%)
Proteinuria	NA	6 (8%)	3 (12%)	1 (4%)
Rash	13 (5%)	19 (25%)	0 (0%)	1 (4%)
Decreased appetite	22 (8%)	1 (1%)	NA	NA



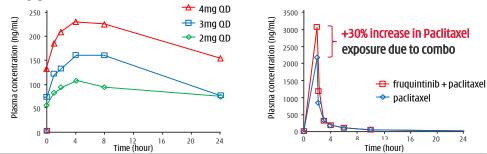
<sup>[1]</sup> Best tumor response for efficacy evaluable patients (patients who had both baseline and post-baseline tumor assessments); ORR = objective response rate; [2] Four PRs not yet confirmed at the time of data cut-off date; mAb = Monoclonal Antibody; [3] Lu, S., et al, "Phase II Study of Fruquintinib plus Gefitinib in Stage IIIb/IV NSCLC Patients Harboring EGFR Activating Mutations", #4780 ESMO Asia, Singapore, November 23, 2019;

<sup>1/4]</sup> Drug discontinuation due to Grade 3 proteinuria and Grade 3 OTC 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 (1025567); an open-label, randomised, multicenter, phase 2 study", The Lancet 2014, 15 (11) 1236-1244.

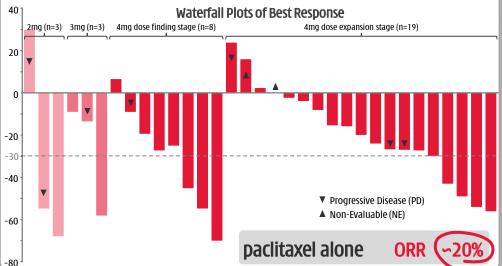
# Fruquintinib - Gastric combo with paclitaxel Phase III initiated Oct 2017 - Interim analysis early 2019



1. Dose proportional increase of fruquintinib AUC at steady state. Over 30% increase in paclitaxel drug exposure (mean AUC<sub>0-8</sub>) 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/m2/week for paclitaxel (98.3% planned dose).

Characteristics (Unit)	Drug Expansion Stage (N=19) Fruquintinib 4 mg + paclitaxel 80 mg/m²			
	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 >3 AEs. Similar to 60% level seen in RAINBOW study of ramcirumab (VEGF mAb) combo with paclitaxel in second-line gastric cancer.

Mith pathtaxel in second line go	astric currect.
Drug related grade 3 or 4 AEs (NCI-CTCAE v 4.0) term	Dose Expansion Stage (N=19) Fruquintinib 4 mg + paclitaxel 80 mg/m²
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%)

## Fruquintinib & surufatinib both unique VEGFR TKIs



### ...potentially ideal VEGFR combo partners for immunotherapy

TKI	1 <sup>st</sup> Generation			2	<sup>1d</sup> Generatio	on	Next G	Next Generation		
Selectivity	Multiple targets R			Relatively selectiv	e	Highly selective	Selective angio-immuno kinase inhibitor			
Inhibitors	Sutent <sup>®</sup>	Nexavar®	Focus V <sup>®</sup>	Fotivda <sup>®</sup>	Lenvima®	Inlyta <sup>®</sup>	Fruquintinib	Surufatinib [1]		
Status	Launched	Launched	Launched	Launched	Launched	Launched	Launched	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 (IC50 < 100nM)	PDGFR <sub>α</sub> PDGFRβ c-Kit Flt3 Ret CSF-1R	Raf-1 b-raf Flt3 P38 c-Kit Ret	PDGFRα PDGFRβ FGFR1-4 c-Kit	PDGFR <sub>\alpha</sub> PDGFR <sub>\beta</sub> EphB2 c-Kit Tie2	PDGFR <sub>\alpha</sub> PDGFR <sub>\beta</sub> FGFR1-4 Ret c-Kit	PDGFR $_{lpha}$ PDGFR $_{eta}$ 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
- Surufatinib inhibits TAM<sup>[2]</sup> production amplifying PD-1 induced immune response



# Lilly amendment - Dec 2018 Secures long-term commercial potential



- Chi-Med will pay full cost of any future development in China. In return, Chi-Med gains:
- Freedom to operate in selecting & pursuing any future indications in China;
- Materially higher milestones & royalties upon launch in new LCI<sup>[1]</sup>;
- Freedom to collaborate with any third-party in clinical development; and
- Possible promotion rights in 30-40% of China for Elunate<sup>®</sup>.<sup>[2]</sup> Not expected before 2021, until then, Lilly responsible for all launch & commercialization costs in China. If we assume promotion rights, we will receive service fees, which we expect to be net income accretive.

	Original 2013 Agreement	Amendment (Dec 2018)
LCI [1] Development Costs - Paid by Lilly	70%	0%
LCI Development Costs – Paid by Chi-Med	30%	100%
LCI Regulatory Approval Milestones – Paid to Chi-Med [3]	12.5	20.0
Royalty Payments – Paid to Chi-Med [4]	15 - 20%	15 - 29%
<b>Co-Promotion Rights in China</b> (% of provinces) <b>Co-Promotion Service Fees</b> – paid to Chi-Med (% Net Sales)	0% 0%	30 - 40% Not disclosed

More control & higher long-term economics on best-in-class asset





Surufatinib

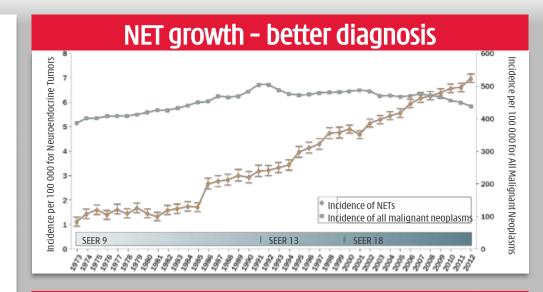
Highly active TKI with unique angio-immuno activity

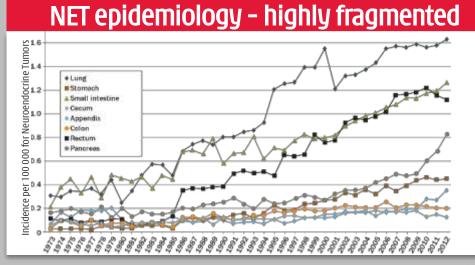
### Surufatinib

### Overview of NET - ~170,000 patients in the U.S. [1][2][3]



- What are neuroendocrine tumors ("NET")?
  - ~2% of all malignancies.
  - Tumor begins in the specialized cells of the body's neuroendocrine system. Cells have traits of both hormone-producing endocrine cells & nerve cells.
  - Found throughout the body's organs. Most NETs take years to develop but some can grow fast.
- Hormone-related symptoms [1]
  - ➤ Functional NETs (~8-35% of patients) release hormones / peptides causing symptoms like diarrhea & flushing; Non-functional NETs have no symptoms.
- S Differentiation & biomarkers for grading:
  - Well differentiated: look like healthy cells grow slowly; Poorly differentiated: look less like healthy cells - grow quickly;
  - Mitotic count Mitosis is process by which tumor cells grow & divide; Ki-67 index - Ki-67 a protein that increases as cells divide.





### High-level NET landscape

### Long-term disease - rapid deterioration in later stages [1][2][3]



#### Grade 1 (G1) NET

Localized / Regional

~8-35% NET patients -Functional NET -Hormone related

> 94% flushing 78% diarrhea 53% heart plaque 51% cramping

symptoms:

Symptoms allow early diagnosis

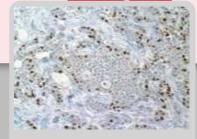
Somatostatin Analogue
Treatment - modulate/
control symptoms
related to hormone
overproduction & tumor
growth:

Octreotide: \$1.6b revenue (2018) Lanreotide: \$1.0b revenue (2018)

#### G1/2 - Advanced NET

Regional / Distant

> mos: 8.3 yrs.



Moderately Differentiated

Ki-67 Index 3-20; Mitotic Count 2-20

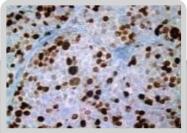
#### G3 - NET/NEC

Distant

## No approved treatments

- exploring *I/O* <sup>[5]</sup>
- + TKI combos

mos: 10 mos.



Poorly Differentiated

Ki-67 Index > 20; Mitotic Count > 20



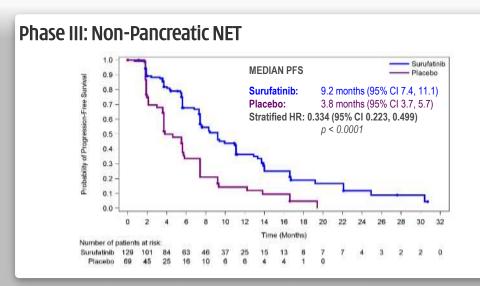
mos:

16.2 yrs.,

**Well Differentiated** *Ki-67 Index* ≤2; *Mitotic Count* <2

### Surufatinib - China data [1] [2]

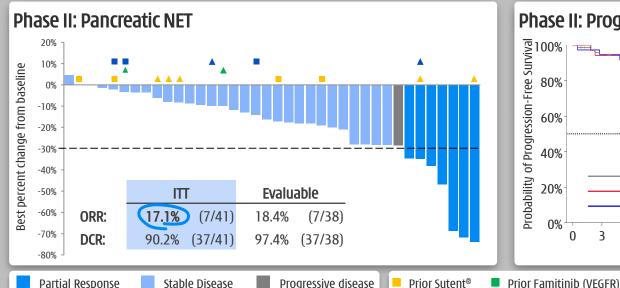
### Broad spectrum NET efficacy incl. Sutent®/Afinitor® failure ptnts.

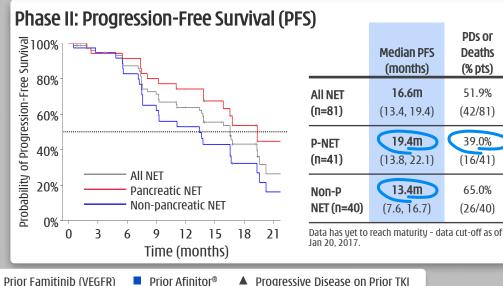


#### Phase III: Safety - Well tolerated - Adverse Events manageable.

Adverse Events ("AEs")	Suru N=129 n (%)	Pbo N=68 n (%)
Any TEAE	127 (98.4)	65 (95.6)
Any Grade ≥3 AE	99 (76.7)	23 (33.8)
Any SAE	34 (26.4)	12 (17.6)
Drug related AE leadi	ng to:	
dose interruption	62 (48.1)	15 (22.1)
dose reduction	62 (48.1)	5 (7.4)
drug withdrawal	23 (17.8)	4 ( 5.9)

	_	
Grade≥3	Suru N=129 n (%)	Pbo N=68 n (%)
Hypertension	47 (36.4)	9 (13.2)
Proteinuria	25 (19.4)	0
Diarrhea	2 (1.6)	0
Bilirubin increased	3 (2.3)	0
AST increased	5 (3.9)	2 ( 2.9)
Hypertriglyceridemia	3 (2.3)	0
ALT increased	4 (3.1)	0
Abdominal pain	1 (0.8)	0
Anemia	9 (7.0)	2 ( 2.9)





Prior Afinitor®

PDs or

Deaths

(% pts)

51.9%

(42/81)

39.0%

(16/41)

65.0%

(26/40)

### Surufatinib - China NET



### NET potential ~\$100-120m/yr. - under treated/diagnosed

### Competitive landscape – *China NET treatments* [1]

Brand	Indication/s	Launched		2017	2018	Q1-2019
SUTENT®	Pancr. NET	2007	Sales (US\$ million)	27	24	7
<i>(sunitinib - VEGFR)</i> Pfizer	(& GIST/RCC)		List Price (US\$/month)	4,455	NRDL Oct-18	2,007
AFINITOR®	Pancr. NET	2013	Sales (US\$ million)	9	13	3
<i>(everolimus - mTOR)</i> Novartis			List Price (US\$/month)	NRDL Jul-17	1,320	1,320
SANDOSTATIN LAR®	GEP-NENS [3]	2003	Sales (US\$ million)	14	15	5
(octreotide - SSA <sup>[2]</sup> ) Novartis			List Price (US\$/month)	1,169	NRDL Oct-18	835

Pancreatic-NET market est. ∽\$10-15m/yr. - Non-Pancreatic NET market ∽5-10X

# Surufatinib - China NET - Phase II (ENETS 2017 [1]) Tumor devascularization & central necrosis

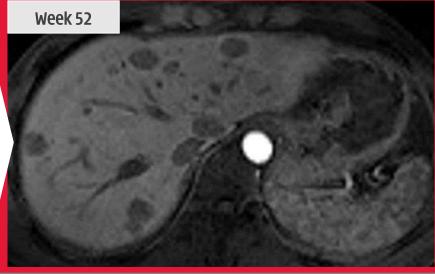


Patient 1

Duodenum NET G2

w/ multiple liver & retroperitoneal lymph node metastases





Patient 2
Rectum NET G2
w/ multiple liver metastases





## SANET-ep vs. RADIANT-4 – cannot compare SANET-ep broader range of tumor origins & later-stage patients



	Asia/China Extra- Pancreatic NET	SANET-ep (n=198) (surufatinib vs placebo)		U.S. Extra- Pancreatic NET	RADIANT-4 (n=302) (everolimus vs placebo)
	Tsai et al. 2013			Yao et al. 2008	
Gastrointestinal Tract	58%	47%	Gastrointestinal Tract	50%	58%
Rectum	30%	27%	Rectum	33%	13%
Stomach	7%	10%	Stomach	8%	4%
Small Intestine	19%	8%	Small Intestine	6%	34%
Other GI	3%	3%	Other Gi	4%	7%
Lung	22%	12%	Lung	21%	30%
Other Organ Site		28%	Thymus		1%
Thymus		7%			
Liver		6%			
Mediastinum		6%			
Adrenal Gland		2%			
Other		8%			
Unknown Origin		14%	Unknown Origin		12%

#### **SANET-ep**

Enrolled more pts with poor prognosis.

		Survival Rate
Primary Site	mos	@ 5-yr
Rectum	2.8y	28%
Stomach	2.4y	32%
Small Intestine	8.6y	69%

#### **RADIANT-4**

**Did not enrol other extra-pancreatic NET organ sites** incl. but not limited to

Throat	Thyroid
Kidney	Ovary
Mediastinum	Adrenal gland
Retroperitoneal	Ampulla vater
Parathyroid gland	Carotid body
Liver	

#### **SANET-ep**

Broader pt. coverage.

#### Pathology grade

**Tumor Origin** 

ECOG PS 0:1

Prior systemic treatment

Multiple organ involvement

2	Grade 1		16%		65%
	Grade 2		84%		35%
	<b>PS 0</b> (treatment : control)		60% (56% : 67%)		74% (73% : 75%)
	<b>PS 1</b> (treatment : control)		40% (44% : 33%)		26% (27% : 26%)
	Any Prior Treatment		67%		61%
	Chemotherapy		40%		25%
	Targeted therapy		10%		none
	Somatostatin Analogues		32%		55%
		66% with multiple organ	involvement		
		76% had liver metastasi	S	79% had liver metastasis	
		47% had lymph nodes metastasis 33% had bone metastasis		43% had lymph nodes me	etastasis
				19% had bone metastasis	;

#### **SANET-ep**

**Later-stage patients**, more heavily pretreated (incl. with targeted therapy) & weaker physical status.

Likely due to later diagnosis in China & availability of everolimus.

22% had lung metastasis

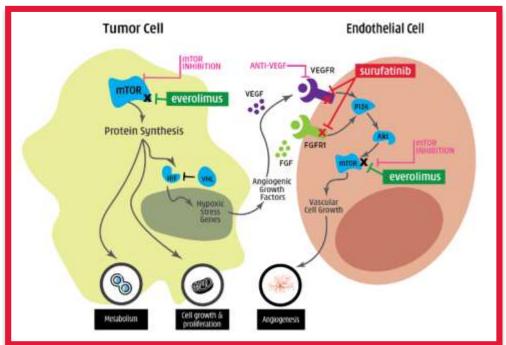
26% had lung metastasis

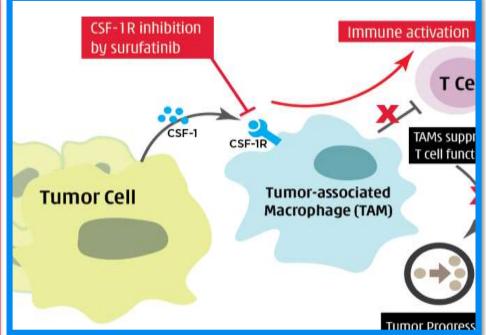


## Very different mechanism of action

**Everolimus** inhibits **mTOR** and blocks the effects caused by the loss of certain genes thereby reducing cell growth, proliferation, and angiogenesis.

Surufatinib inhibits VEGFR1/2/3 and FGFR1 blocking vascular cell growth and angiogenesis; as well as CSF-1R which limits the production of TAMs which cloak the cancer cell from T-Cell attack.





## ~170,000 NET patients in U.S. [1][2]

### U.S. NET treatment landscape - highly fragmented



		Somatostatin Based Therapies	;	K	inase Inhibitor Therapies	
	Sandostatin® LAR (octreotide)	Somatuline Depot® (lanreotide)	Lutathera <b>®</b> ( <sup>177</sup> Lu-Dotatate)	Afinitor® (everolimus)	Sutent® (sunitinib)	Surufatinib (China NDA accepted)
2018 Sales	\$1.6bn	\$1.0bn	\$0.17bn	\$1.6bn	\$1.0bn	-
MOA [3]	Somatostatin analogue	Somatostatin analogue	Somatostatin receptor targeting radiotherapy	mTOR inhibition	Inhibits multiple receptor tyrosine kinases	VEGFR/FGFR1 & CSF-1R inhibition
Admin.	Subcutaneous or intramuscular inj. (LAR)	Subcutaneous injection	Subcutaneous injections (radioqualified physicians).	Oral tablet	Oral capsules	Oral capsules
Shelf-life	3 years	2 years	72 hours	3 years	3 years	2+ years <sup>[5]</sup>
Dosage	2 wks: Sando. inj. 0.1-0.6mg per day; then 2 months Sando. LAR 20mg per 4 wks.	120mg inj. every 4 wks.	7.4GBq (one ∽25ml vial) inj. every 8 wks - 4 doses total.	10mg orally once daily.	37.5mg taken orally once daily.	300mg orally once daily.
NET indication/s	<ul> <li>LT treatment of severe diarrhea &amp; flushing from meta. carcinoid tumors.</li> </ul>	<ul> <li>GEP-NETs: unresectable, well or moderately diff., (locally adv. or meta) GEP-NETs to improve PFS.</li> <li>Carcinoid Syndrome: to reduce frequency of short-acting somatostatin rescue therapy.</li> </ul>	<ul> <li>Somatostatin receptor- positive GEP-NETs.</li> </ul>	<ul> <li><u>pNET</u>: progressive pNET (unresectable, locally adv. or meta).</li> <li><u>GI-NET or Lung NET</u>: progressive, well-diff., <i>non-functional</i> NET (unresectable, locally adv. or meta). Not for <i>functional</i> carcinoid tumors.<sup>[4]</sup></li> </ul>	<ul> <li><u>pNET</u>: Progressive, well- differentiated pNETs (unresectable locally adv. or meta).</li> </ul>	<ul> <li><u>Non-pNET</u>: SANET-ep study was in low- or intermediategrade adv. non-pancreatic NET.</li> <li><u>pNET</u>: Phase III ongoing.</li> </ul>
Non-NET indication/s	<ul> <li>Acromegaly; watery diarrhea from VIPomas.</li> </ul>	• Acromegaly.		<ul> <li>Adv. HR+ HER2-n breast cancer; adv. 2L RCC; renal angiomyolipoma and TSC.</li> </ul>	<ul> <li>2L GIST; adv. RCC; high risk of recurrent RCC.</li> </ul>	

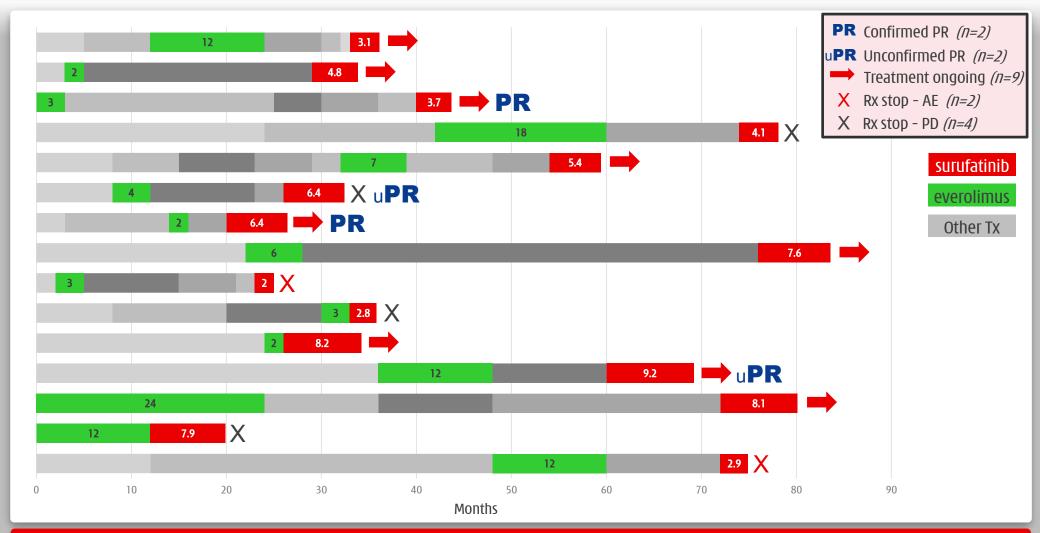
	Sandostatin®/ Placebo	Somatuline Depot® / Placebo	Lutathera®+Sando.LAR/ Sando.LAR		tor®/ cebo	Sutent®/ Placebo		ufatinib/ Hacebo
mPFS (mo.) primary EP	14.3 / 6.0	NR / 18.0	NR / 8.5	pNET 11.0 / 4.6	Lung & GI NET 11.0 / 3.9	pNET: 11.4 / 5.5	Ph II pNET 19.4	Ph III non-pNET 9.2 / 3.8
HR	0.34	0.47	0.21	0.35	0.48	0.42	Ph III	0.33
( <i>p-value</i> )	0.000072	⟨0.001	(0.0001	(0.001	(0.001	⟨0.001	Ongoing	(0.0001
ORR	2% / 2%	NR	18% / 3%	5% / 2%	2% / 1%	9% / 0%	17% (Ph II)	10.3%
DCR	69% / 40%	NR	95% / 76%	73% / 51%	81% / 64%	72% / 60%	90% (Ph II)	87%
Pivotal Trial	PROMID	CLARINET	NETTER-1	RADIANT-3	RADIANT-4	A6181111	SANET-p	SANET-ep

[1] Dasari A, et al.: Trends in the Incidence, Prevalence, & Survival Outcomes in Patients With Neuroendocrine Tumors in the U.S.. JAMA Oncol. 2017;3(10):1335-1342; [2] www.cancer.net (patient information from ASCO) - NET is a subtype of neuroendocrine neoplasms, NENs); [3] MOA = Mechanism of Action; [4] Afinitor is only approved for pancreatic neuroendocrine tumors in China; [5] 2-year stability studies completed so far; mPFS = median progression-free survival; HR = Hazard Ratio; ORR = objective response rate; DCR = Disease control rate.

95

# Surufatinib efficacy post everolimus failure U.S. Phase Ib (n=15) - pNET duration of treatment





Encouraging preliminary surufatinib efficacy post everolimus failure - different MOA[1]





HMPL-523 (Syk) & HMPL-689 (PI3Kδ)

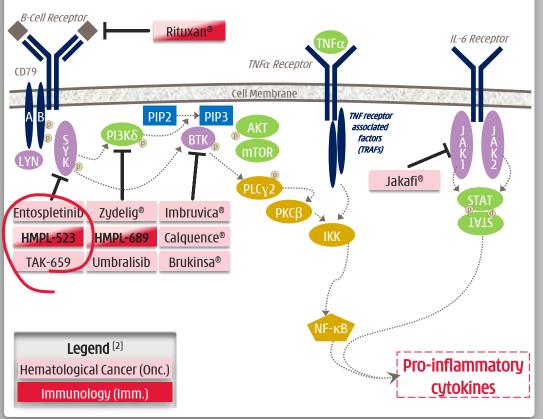
Potential first-in-class (Syk) & best-in-class (PI3K $\delta$ ) assets

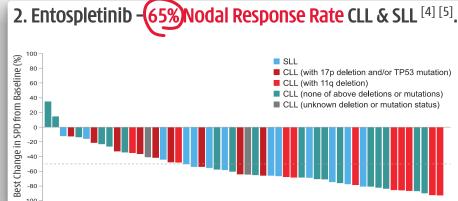
# HMPL-523 – hematological malignancies Syk exciting target emerging – Lymphoma PoC ongoing



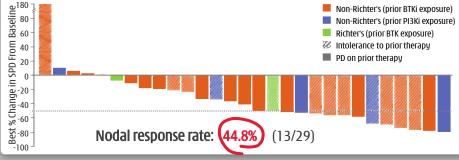
1. The B-cell signaling is **critical in hematological cancer** with three **breakthrough therapies** recently approved.

2018 sales: Imbruvica® \$6.2bn; Zydelig® \$0.1bn; Jakafi® \$2.4bn; & Rituxan® \$5.3bn [1].









- 4. Entospletinib not a perfect compound [6].
- Poor solubility/oral absorption & high variation in drug exposure.
- Some CYP <sup>[6]</sup> inhibition & increased risk of drug-drug interaction.
- 66% Grade  $\geq$ 3 AEs, 49% SAEs; 46% drug interruption & 20% disco.

### HMPL-523 (Syk) in hematological cancer Australia & China – large Ph.Ib expansion. US/EU Ph.I imminent



- Extensive Ph.I dose escalation study now complete in Australia & China (total n=60);
- RP2D<sup>[1]</sup> determined & large Ph. Ib dose expansion study, total n=192, underway in 13 active sites in Australia & China;
- Phase I/Ib data set currently > 150 patients;
- US IND application cleared by FDA
   & U.S./E.U. Phase I imminent;
- Plan to initiate China registration studies in 2019.

## Australia & China Phase I/Ib studies

#### Stage I: dose escalation

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



N = 33

N = 27

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 (PRC)

#### ...Now enrolling



until disease progression, death, intolerable toxicity, etc.

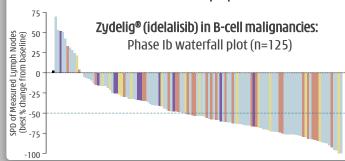
[1] RP2D = Recommended Phase II doses.

# HMPL-689 – Phase I Australia & China ongoing Designed to be a best-in-class inhibitor of PI3K $\delta$



#### 1. PI3K $\delta$ now a proven target.

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



#### 2. PI3K $\delta$ inhibitors being developed in a very broad range of indications.

Compound		Indication	Status	Issue
Zydelig <sup>®</sup> (idelalisib) PI3Kδ	Gilead	Chronic lymphocytic leukaemia, non-Hodgkin's lymphoma	Marketed	<b>High incidence of liver toxicity</b> 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®		Relapsed or refractory chronic lymphocytic leukaemia / small lymphocytic lymphoma	Approved	<b>Need to spare PI3Kγ</b> serious infection seen &
(duvelisib) PI3Kγ/δ		Relapsed or refractory follicular lymphoma	Approved [2]	associated with a boxed warning for 4 fatal and/or
		Peripheral T-cell lymphoma	Phase II enrolling	serious toxicities
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 PI3K $\delta$  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®	<sup>®</sup> aqopilA
РІЗКδ	0.8 (n = 3)	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 (142x)	104 <b>(52x)</b>	2 (2X)	6.4 <b>(9x)</b>
PI3K $\alpha$ (fold vs. PI3K $\delta$ )	>1,000 <b>(&gt;1,250x)</b>	866 <b>(433x)</b>	143 <b>(143x)</b>	0.5 (1X)
PI3Kδ human <u>whole blood</u> CD63+	3	14	15	n/a
PI3Kβ (fold vs. PI3Kδ)	87 <b>(109x)</b>	293 <b>(147x)</b>	8 (8X)	3.7 <b>(5x)</b>





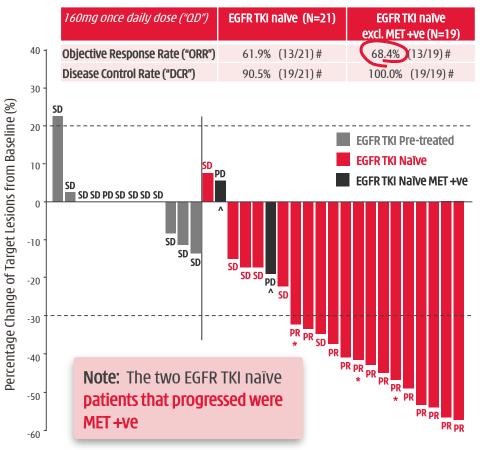
Epitinib (EGFR), Theliatinib (EGFRwt) & HMPL-453 (FGFR)

Aim to establish proof-of-concept

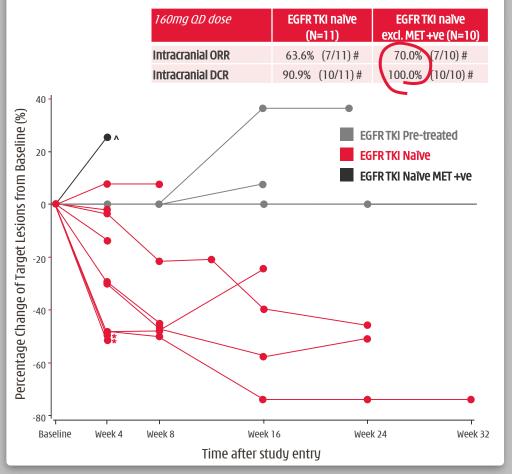
## Epitinib - 70% response in NSCLC w/ brain mets[1] Unmet medical need. Investment case under review.



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







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

## Epitinib - Safe & well tolerated



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%)

(Drug related AL3 reported 7 10/0)				
160mg QD dose	All Grades n (%)	Grade 3/4 n (%)		
Skin rash	21 (60.0%)	1 (2.9%)		
Diarrhea	12 (34.3%)	-		
AST increase	12 (34.3%)	1 (2.9%)		
ALT increase	11 (31.4%)	1 (2.9%)		
Total bilirubin increase	10 (28.6%)	2 (5.7%)		
Stomatitis	5 (14.3%)	-		
Exfoliative dermatitis	5 (14.3%)	-		
Pruritus	5 (14.3%)	-		
Hyper-pigmentation	4 (11.4%)	-		
Gamma-GGT increase	4 (11.4%)	2 (5.7%)		
Conjugated hiliruhin	4 (11 4%)	1 (2 9%)		

160mg QD dose	All Grades n (%)	Grade 3/4 n (%)
Skin rash	31 (83.8%)	2 (5.4%)
Hyper-pigmentation	18 (48.6%)	1 (2.7%)
ALT increase	15 (40.5%)	7 (18.9%)
AST increase	15 (40.5%)	4 (10.8%)
ASP increase	11 (29.7%)	1 (2.7%)
Diarrhea	10 (27.0%)	-
Proteinuria	10 (27.0%)	-
Total bilirubin increase	9 (24.3%)	1 (2.7%)
Hyperuricemia	9 (24.3%)	2 (5.4%)
Gamma-GGT increase	7 (18.9%)	4 (10.8%)
Stomatitis	6 (16.2%)	-

- 4. 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
- 1st-line chemo naïve
- 120mg QD dosage
- 25 weeks (177 days) on treatment with clear response in multiple measurable (>10mm diameter) brain lesions









### Theliatinib Potent & highly selective TKI - strong affinity to EGFRwt kinase



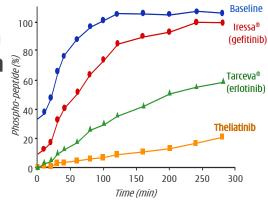
#### 1. Major unmet medical need for wild-type EGFR activation tumors.

- EGFR TKIs are less effective in solid tumors with wild-type EGFR activation (gene amplification & protein over expression).
- Ph.Ib study in esophageal cancer short-term response & stable disease observed. Does not warrant continued development as monotherapy. Consider potential immunotherapy combo.

Tumor Types	Wild-type: Gene Amplification	Wild-type: Over Expression	Mutations	<b>TKIs approved:</b> Iressa®, Tarceva®
NSCLC	29%	62%	10-30%	llessa*, laiteva*
Esophagus	8-30%	30-90%	12% (esophageal adenoc	arcinoma)
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)
			MAbs approved: Erbitux®, Vect	:ibix®

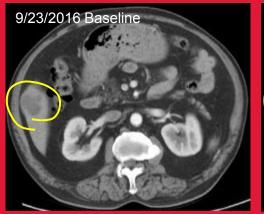
## 2. Superior anti-tumor activity of theliatinib in pre-clinical studies with wild-type EGFR. 5-10-fold more potent than Tarceya®

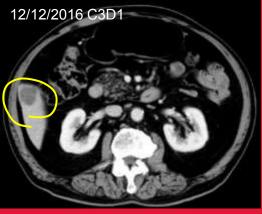
- than Tarceva®.
- Sustained target occupancy.



### CASE STUDY - EGFR protein over expression

- May 4, 2016: Man, 62, stage IV esophageal squamous cell cancer cT3N0M1with 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 theliatinib 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).

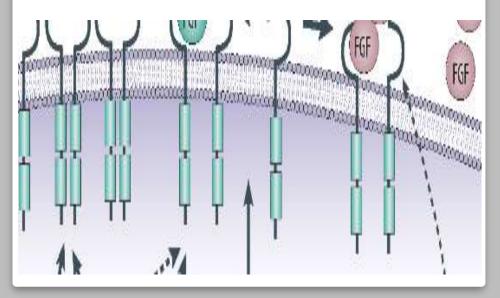




# HMPL-453 – Phase I in China ongoing Designed as best-in-class FGFR1/2/3 inhibitor



- 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.

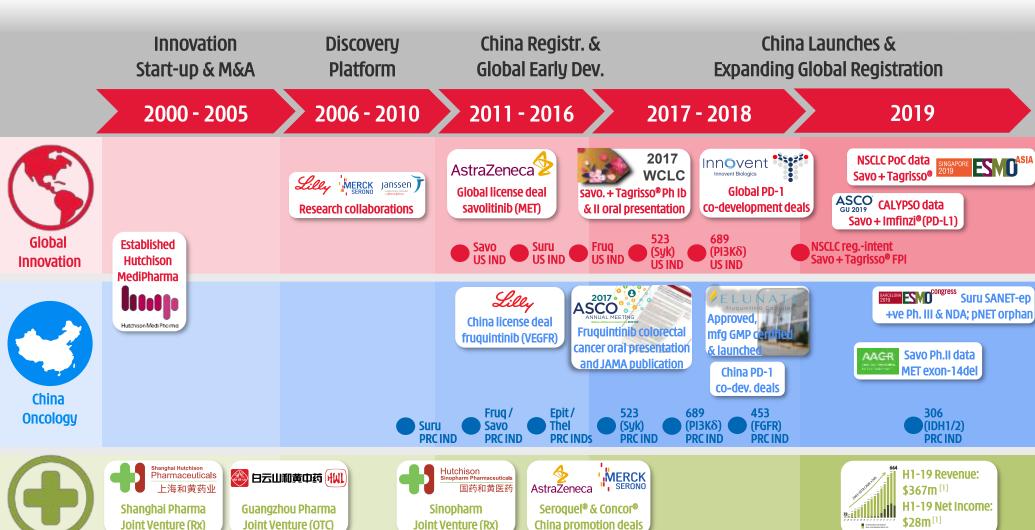
	Gene amplification	Gene translocation	Gene mutation
FGFR1	Lung squamous (7~15%)  H&N squamous (10~17%)  Esophageal squamous (9%)  Breast (10~15%)	Lung squamous (n/a) Glioblastoma (n/a) Myeloproliferative syndrome (n/a) Breast (n/a)	Gastric (4%) Pilocytic astrocytoma (5~8%)
FGFR2	Gastric (5~10%) Breast (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%)



A3 Further Corporate Information

## Important milestones in Chi-Med's evolution





~1,300 Med.

Sales Reps.

<100 Med.

Sales Reps.

**Existing China** 

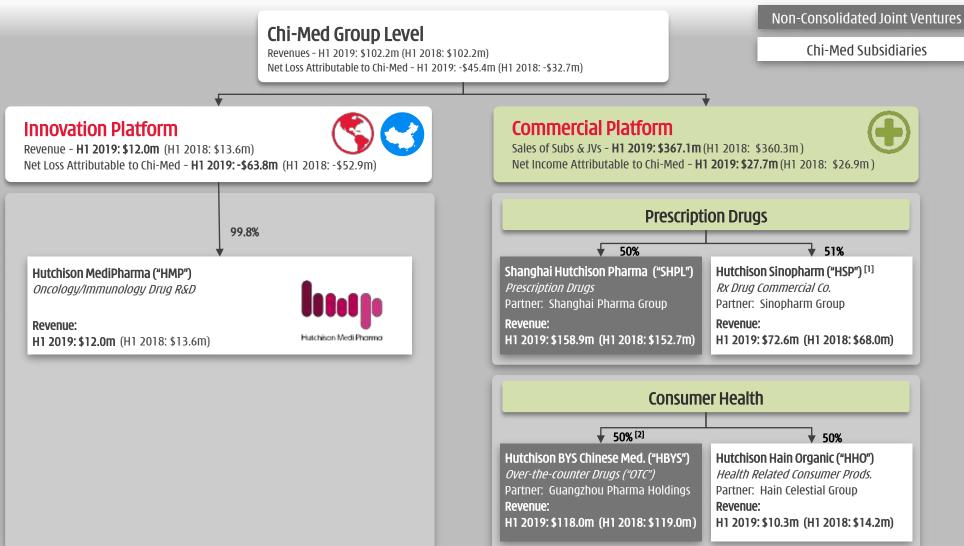
Business

~2,400 Med.

Sales Reps.

## CHI-MED

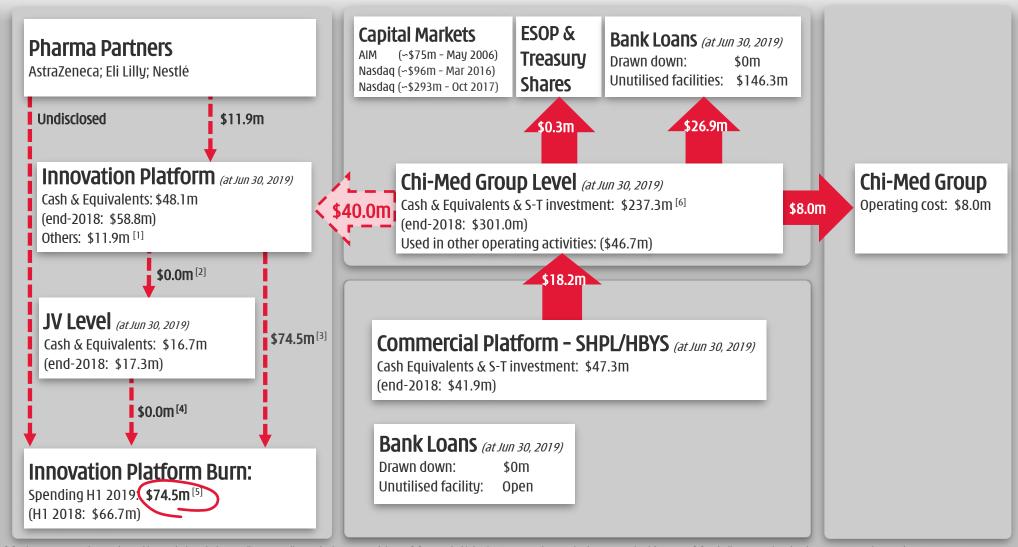
### Chi-Med Group Structure - Major Entities



## FY2019 H1 Inter-group cash flow



### \$237.3m cash (Jun 30, 2019); \$146.3m in undrawn bank facilities



[1] Others represent changes in working capital, capital expenditure spending and other non-cash items; [2] No capital injection to NSP and no service income received from NSP; [3] Including research & development cost and general & admin. expenses; [4] Share of NSP operating loss; [5] Please see appendix "Non-GAAP Financial Measures and Reconciliation" for a Reconciliation of GAAP to adjusted research and development expenses; [6] Including \$153.9m short-term investment (deposits over 3 months) as at June 30, 2019.

# Non-GAAP Financial Measures and Reconciliation (1/3)



Reconciliation of Adjusted Group net cash flows and Adjusted Group net cash flows excluding financing activities:

	Jun 30, 2019	2019 Current Guidance	2019 Previous Guidance
Cash and cash equivalents and short-term investments at end period	237.3	180-210 [1]	150-180 [1]
Less: cash and cash equivalents and short-term investments at beginning of year	(301.0)	(300)	(300)
Adjusted Group net cash flows	(63.7)	(90) - (120)	(120) - (150)
Add: Net cash used in financing activities for the period	29.5	_[1]	_[1]
Adjusted Group net cash flows excluding financing activities	(34.2)	(90) - (120)	(120) - (150)

#### Reconciliation of Adjusted Research and Development Expenses:

	H1 2018	H1 2019
Segment operating loss – Innovation Platform	(53.1)	(63.9)
Less: Segment revenue from external customers - Innovation Platform	(13.6)	(12.0)
Add: Costs of goods & service - third parties	_	1.4
Adjusted R&D expenses	(66.7)	(74.5)

# Non-GAAP Financial Measures and Reconciliation (2/3)



	Six Month	is Ended	Gr	owth Amoun	t	Growth %			
\$'Million (except %)	June 30, 2019	June 30, 2018	Actual	at CER	Exchange effects	Actual growth %	CER growth %	Exchange effect %	
Consolidated sales	102.2	102.2	-	5.1	(5.1)	0%	5%	-5%	
Commercial Platform	90.2	88.6	1.6	6.4	(4.8)	2%	7%	-5%	
<ul> <li>Prescription Drugs subsidiary</li> </ul>	72.6	68.0	4.6	9.1	(4.5)	7%	13%	-6%	
<ul> <li>Consumer Health subsidiaries</li> </ul>	17.6	20.6	(3.0)	(2.7)	(0.3)	-15%	-13%	-2%	
Non-consolidated joint venture sales	276.9	271.7	5.2	22.3	(17.1)	2%	8%	-6%	
- SHPL	158.9	152.7	6.2	15.8	(9.6)	4%	10%	-6%	
- HBYS	118.0	119.0	(1.0)	6.5	(7.5)	-1%	5%	-6%	
Total Commercial Platform (Non-GAAP)	367.1	360.3	6.8	28.7	(21.9)	2%	8%	6%	
Consolidated net income attributable to Chi- Med	(45.4)	(32.7)	(12.7)	(15.6)	2.9	-39%	-48%	9%	
Innovation Platform	(63.8)	(52.9)	(10.9)	(15.4)	4.5	-21%	-29%	8%	
Commercial Platform	27.7	26.9	0.8	2.4	(1.6)	3%	9%	-6%	
— Prescription Drugs	21.8	20.8	1.0	2.3	(1.3)	5%	11%	-6%	
— Consumer Health	5.9	6.1	(0.2)	0.1	(0.3)	-4%	2%	-6%	
Sales of SXBX pill	141.0	129.8	11.2	19.7	(8.5)	9%	15%	-6%	

# Non-GAAP Financial Measures and Reconciliation (3/3)



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

- 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).

					IFF	RS								US GA	AP				H1'18- H1'19
(US\$ millions)	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	H1'18	H1'19	
Sales (Non-GAAP)	21.9	27.9	65.1	101.4	119.0	155.8	197.0	236.4	278.6	360.7	402.3	465.4	518.9	627.4	677.2	664.4	360.3	367.1	2%
Prescription Drugs	17.2	21.8	23.3	23.2	28.1	39.5	54.4	71.2	92.4	116.5	138.2	204.9	286.6	<i>372.3</i>	411.0	408.5	220.7	231.5	5%
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	50.2	105.5	149.9	166.4	132.8	68.0	72.6	7%
- 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	275.7	<i>152.7</i>	158.9	4%
Consumer Health	4.7	6.1	41.8	78.2	90.9	116.3	142.6	165.2	186.2	244.2	264.1	260.5	232.3	255.1	266.2	255.9	139.6	135.6	-3%
- Consolidated subsidiaries	4.7	6.1	9.3	8.9	<i>3.7</i>	5.5	7.0	14.1	14.9	15.5	16.5	16.8	20.7	31.0	38.8	40.1	20.6	17.6	-15%
- 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	215.8	119.0	118.0	-1%
Total Sales Growth	n/a	27%	133%	56%	17%	31%	26%	20%	18%	29%	n/a	16%	11%	21%	8%	-2%		2%	
- GuanBao divested in Sept'2017	-	-	-	-	-	-	-	-	(11.4)	(50.5)	(51.6)	(49.7)	(40.7)	(45.0)	(38.6)	0.0	0.0	0.0	n/a
Adjusted Consumer Health	4.7	6.1	41.8	78.2	90.9	116.3	142.6	165.2	174.8	193.7	212.5	210.8	191.6	210.1	227.6	255.9	139.6	135.6	-3%
- Adjusted Non-consolidated joint venture	0.0	-	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	215.8	119.0	118.0	-1%
Adjusted Sales (Non-GAAP)	21.9	27.9	65.1	101.4	119.0	155.8	197.0	236.4	267.2	310.2	<i>350.7</i>	415.7	478.2	582.4	638.6	664.4	360.3	367.1	2%
Total Adjusted Sales Growth	n/a	27%	133%	56%	17%	31%	26%	20%	13%	16%	13%	19%	15%	22%	10%	4%		2%	
Net (loss)/Income after tax (Non-GAAP)	(10.7)	(3.6)	2.2	6.7	11.2	14.7	21.5	27.9	30.1	33.1	39.7	48.8	54.1	63.3 [3	77.3 [4]	83.6	55.1	57.0	3%
Prescription Drugs	(0.4)	1.3	1.9	1.3	1.9	2.8	6.0	11.9	14.2	<i>17.7</i>	22.4	26.5	31.9	41.4	53.0	63.9	41.5	43.7	5%
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	0.1	0.6	1.6	2.4	4.1	2.7	1.6	-41%
- Non-consolidated joint venture	(0.4)	1.3	1.9	1.3	1.9	2.8	6.0	11.9	14.2	17.7	22.4	26.4	31.3	39.8	50.6	59.8	38.8	42.1	9%
Consumer Health	(10.3)	(4.9)	0.3	5.4	9.3	11.9	15.5	16.0	15.9	15.4	17.3	22.3	22.2	21.9	24.3	19.7	13.6	13.3	-2%
- Consolidated subsidiaries	(10.3)	(4.9)	(2.9)	(2.4)	0.2	-	0.8	1.0	(0.4)	(1.1)	0.1	1.5	0.8	1.5	3.5	2.8	1.6	1.1	-29%
- Non-consolidated joint venture	-	-	3.2	7.8	9.1	<i>11.9</i>	14.7	15.0	<i>16.3</i>	16.5	17.2	20.8	21.4	20.4	20.8	16.9	12.0	12.2	2%
% Margin	-48.9%	-12.9%	3.4%	6.6%	9.4%	9.4%	10.9%	11.8%	10.8%	9.2%	9.9%	10.5%	10.4%	10.1%	11.4%	12.6%	15.3%	15.5%	
Net (loss)/income attrib. to Chi-Med	(5.7)	(3.7)	(0.5)	1.2	4.5[2]	5.9[2]	9.3[2]	12.6[2	13.6 [2]	14.6[2]	18.2 [2]	22.8[2]	25.2[2]	29.9[3	37.5[4]	41.4	26.9	27.7	3%
Prescription Drugs	(0.2)	0.6	1.0	0.7	0.9	1.4	3.0	5.9	7.1	8.8	11.2	13.2	15.9	20.7	26.5	32.1	20.8	21.8	5%
Consumer Health	(5.5)	(4.3)	(1.5)	0.5	3.6	4.5	6.3	6.7	6.5	5.8	7.0	9.6	9.3	9.2	11.0	9.3	6.1	5.9	-4%
Net (loss)/income attrib. to Chi-Med growth	n/a	-35%	-86%	340%	275%	31%	58%	35%	8%	7%	n/a	26%	10%	19%	25%	10%		3%	

<sup>[1] 2003–2006</sup> incl. disco. operation; [2] Continuing Operations; [3] Excludes the land compensation in SHPL of \$80.8 million from net income after tax and \$40.4 million from net income attributable to Chi-Med for 2016; [4] Excludes SHPL's R&D related subsidies of \$5.0 million from net income after tax and \$2.5 million from net income attributable to Chi-Med for 2017.



### 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 median PE multiples is approximately \$1.8 billion. [1] Given our share in the JVs, Chi-Med's share of this value is approximately \$0.9 billion.

			NET SALES			NET INCO	OME		VALUATION	[4]
	Code	2017 Jan-Dec	2018 Jan-Dec	FY17-18 Growth	2017 Jan-Dec	2018 Jan-Dec	FY17-18 Growth	FY2018 Margin	Market Cap.	P/E
CHI-MED Commercial Platform Subsidiaries/JVs <sup>[2]</sup>		<b>638.6</b> <sup>[3]</sup>	664.4	4%	77.3	83.6	8%	13%	n/a	n/a
Li Zhu Pharma	000513	1,292.6	1,342.5	4%	124.2	179.0	44%	13%	3,590	16
Shandong Dong E E Jiao	000423	1,117.0	1,111.9	0%	309.7	316.2	2%	28%	3,384	12
Kunming Pharma	600422	886.7	1,076.1	21%	50.8	51.8	2%	5%	1,247	23
Zhejiang Kang En Bai Pharma	600572	802.1	1,028.3	28%	110.6	122.5	11%	12%	2,655	24
Tianjin Zhong Xin Pharma	600329	862.0	963.4	12%	71.7	86.0	20%	9%	1,560	18
Zhangzhou Pien Tze Huang	600436	562.7	722.1	28%	118.2	171.0	45%	24%	9,654	52
Jiangsu Kang Yuan	600557	496.2	579.4	17%	57.3	66.3	16%	11%	1,333	20
Zhuzhou Qian Jin Pharma	600479	482.2	504.3	5%	37.4	45.8	23%	9%	618	15
Jiu Zhi Tang	000989	581.3	473.1	-19%	109.3	49.0	-55%	10%	1,113	27
Wuhan Jian Min Pharma	600976	410.8	327.5	-20%	13.9	12.3	-11%	4%	356	29
Peer Group Median (10 Comps. excl. Chi-Med)		691.7	842.8	22%	90.5	76.2	-16%	9%	1,446	21
All 61 Listed thina Pharma. Companies Median		515.1	579.4	12%	50.8	49.6	-2%	9%	1,247	21

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 2018 Net Sales in the  $\sim$ \$300-1,400 million range.

(US\$ millions)

# National Reimbursement Drug List Pricing ("NRDL") July'17 update – 15 new drugs in oncology<sup>[1]</sup> added to NRDL



		l	Jnit Pricing (US\$	) [3]		Approximate Mor	thly Pricing (U	S\$) <sup>[3]</sup>	
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	$\Delta$ %	Dosage	Avg. Tender	Reimbursed	Indication coverage
Herceptin® (trastuzumab)	Roche	440mg:20ml	\$3,298.81	\$1,125.93	-66%	Breast: 4mg/kg wk 1, 2mg/kg weekly. <sup>[2]</sup>	\$4,500	\$1,540	Breast: Her2+; Her2+ meta. Her2+ late-stage meta. gastric.
Avastin® (bevacizumab)	Roche	100mg:4ml	\$772.74	\$296.00	-62%	10mg/kg Q2W.	\$11,590	\$4,440	Late-stage meta. CRC or advanced non-squamous NSCLC.
TheraCIM <sup>®[4]</sup> (nimotuzumab)	Biotech Pharma	50mg:10ml	\$435.26	\$251.85	-42%	100mg weekly.	\$3,730	\$2,160	Combo with radiotherapy for EGFR+ Stage III/IV nasopharyngeal carcinoma.
Rituxan® (rituximab)	Roche	500mg:50ml <sup>[2]</sup>	\$2,544.74	\$1,228.15	-52%	375 mg/m² weekly.	\$13,090	\$6,320	Restorative or resistant follicular central type lym.; CD20+ stage III-IV follicular NHL, CD20+ DLBCL.
Tarceva® (erlotinib)	Roche	150mg <sup>[2]</sup>	\$68.15	\$28.89	-58%	150mg QD.	\$2,040	\$870	Advanced NSCLC with limited EGFR gene mutation.
Nexavar® (sorafenib)	Bayer	0.2g	\$60.44	\$30.07	-50%	400mg BID.	\$7,250	\$3,610	Unresectable RCC. Unresectable HCC. meta. Diff. thyroid after radio-iodine therapy.
Tykerb® (lapatinib)	GSK	250mg	\$17.63	\$10.37	-41%	1,500mg QD.	\$3,170	\$1,870	Adv./meta. breast cancer with Her2 O/E, after anthracycline, paclitaxel, trastuzumab.
AiTan® (apatinib)	Hengrui	<b>425mg</b> <sup>[2]</sup>	\$47.85	\$30.22	-37%	850mg QD.	\$2,870	\$1,810	3L gastric adenocarcinoma or esophageal junction with adenocarcinoma.
Velcade® (bortezomib)	J&J	3.5mg <sup>[2]</sup>	\$1,873.78	\$906.07	-52%	1.3mg/m² quartic every 3 wks.	\$6,360	\$3,080	Myeloma; recurring or refractory mantle cell lymphoma.
EnDu® (rh-endostatin)	Simcere	15mg	\$132.15	\$93.33	-29%	7.5mg/m² iv QD 2-wks- on / 1-week-off.	\$2,110	\$1,490	Late-stage NSCLC.
Epidaza® (chidamide)	Chipscreen	5mg	\$81.48	\$57.04	-30%	30mg QD, 2x per wk.	\$4,190	\$2,930	2L+ Recurring or refractory peripheral T-cell lymphoma (PTCL).
Zytiga® (abiraterone)	J&J	250mg	\$45.63	\$21.48	-53%	1,000mg QD.	\$5,480	\$2,580	Metastatic or ovariectomized prostate cancer.
Faslodex® (fulvestrant)	AstraZeneca	250mg:5ml	\$806.81	\$355.56	-56%	500mg per month.	\$1,610	\$710	Advanced ER/PR+ breast can., failing aromatase inhibitor.
Afinitor® (everolimus)	Novartis	5mg <sup>[2]</sup>	\$36.44	\$21.93	-40%	10mg QD.	\$2,190	\$1,320	Adv. RCC after sunitinib or sorafenib. Adv./meta. pancreatic NETs. Tuberous sclerosis with renal angiomyolipoma.
Revlimid (lenalidomide)	Celgene	25mg <sup>[2]</sup>	\$413.93	\$163.26	-61%	25mg QD 3-wks-on/ 1-wk-off.	\$9,310	\$3,670	2L+ Recurring myeloma.

# National Reimbursement Drug List Pricing ("NRDL") Oct'18 update - 17 new drugs in oncology added to NRDL



			Unit Pricing (l	JS\$) <sup>[2]</sup>		Approximate Monthly F	Pricing (US\$) <sup>[2]</sup>		
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	$\Delta$ %	Dosage [1]	Avg. Tender	Reimbursed	Indication coverage
Focus V <sup>®</sup> (anlotinib)	Sino Biopharn	n 12mg	\$127	\$70	-45%	12mg QD (2 wks-on/1-wk-off)	\$1,783	\$981	3L NSCLC
Oncaspar® (pegaspargase)	Hengrui	5ml:3750 IU	\$560	\$429	-23%	≤2ml every 14 days	\$1,231	\$943	1L ALL
Vidaza <sup>®</sup> (azacitidine)	Celgene	100mg	\$378	\$152	-60%	1 <sup>st</sup> cycle: 75mg QD for 7 days; 4wk cycle. After 2 cycles increase dose to 100mg, min of 4-6 cycles	\$14,022	\$5,636	Refractory anemia (RA) or RA with ringed sideroblasts (RARS), RA with excess blasts (RAEB / RAEB-T), and chronic myelomonocytic leukemia (CMMoL)
Inlyta® (axitinib)	Pfizer	5mg	\$99	\$30	-70%	5mg BID	\$5,957	\$1,787	2L Advanced renal cell carcinoma
Tagrisso® (osimertinib)	AstraZeneca	80mg	\$253	\$73	-71%	80mg QD	\$7,597	\$2,201	EGFR TKI refractory T790M+ NSCLC
Ninlaro® (ixazomib)	Takeda	4mg	\$3,234	\$710	-78%	4mg on Days 1, 8, 15 (28 day cycle)	\$12,934	\$2,839	2L Multiple myeloma
Xalkori <sup>®</sup> (crizotinib)	Pfizer	250mg	\$123	\$37	-70%	250mg BID	\$7,407	\$2,245	Locally adv. or meta. ALK+ or ROS1+ NSCLC
Gilotrif <sup>®</sup> (afatinib)	Boehringer	40mg	\$116	\$29	-75%	40mg QD	\$3,483	\$863	NSCLC with EGFR
Tasigna® (nilotinib)	Novartis	200mg	\$39	\$14	-65%	400mg BID	\$4,645	\$1,635	CML
Votrient® (pazopanib)	Novartis	200mg	\$66	\$23	-65%	800mg QD	\$7,891	\$2,348	RCC
Sutent <sup>®</sup> (sunitinib)	Pfizer	12.5mg	\$49	\$22	-55%	GIST & RCC: 50mg QD pNET: 37.5mg QD	\$5,544 \$4,455	\$2,498 \$2,007	RCC, GIST, pNET
Stivarga® (regorafenib)	Bayer	40mg	\$52	\$28	-46%	160mg QD, 3-wks-on/1-wk-off *	\$4,368	\$2,352	Meta. CRC, GIST, HCC
Zykadia <sup>®</sup> (certinib)	Novartis	150mg	\$108	\$28	-74%	450mg QD	\$9,699	\$2,564	NSCLC
Zelboraf <sup>®</sup> (vemurafenib)	Roche	240mg	\$30	\$16	-47%	960mg BID	\$7,252	\$2,369	Melanoma
Erbitux® (cetuximab)	Merck	100mg	\$571	\$186	-67%	400mg/m2 initial dose, 250mg weekly	\$10,446	\$3,074	Colorectal cancer, head and neck cancer
Sandostatin LAR <sup>®</sup> (octreotide)	Novartis	20mg	\$1,169	\$835	-29%	20mg Q4W	\$1,169	\$835	GEP-NENS
Imbruvica <sup>®</sup> (ibrutinib)	JNJ	140mg	\$78	\$27	-65%	MCL: 560mg QD CLL & WM: 420mg QD	\$9,324 \$6,993	\$3,263 \$2,447	MCL, CLL/SLL

# National Reimbursement Drug List Pricing ("NRDL") Nov'19 update - 8 new & 9 renewed drugs in oncology<sup>[1]</sup>



			Unit Pricing (	US\$) <sup>[3]</sup>	Approximate Mo	nthly Pricing (U	IS\$) <sup>[3]</sup>	
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed $\Delta\%$	Dosage	Avg. Tender	Reimbursed	Indication coverage
Elunate <sup>®</sup> (fruquintinib)	Chi-Med	5mg	\$149	\$53.77 -64%	5mg QD 3wks/1wk-off.	\$3,350	\$1,210	Metastatic colorectal cancer, 3L
Tyvyt <sup>®</sup> (sintilimab)	Innovent	10ml	\$1,114	\$404.41 -64%				Classical Hodgkin's lymphoma, 3L
Saiweijian <sup>®</sup> (raltitrexed)	Sino Biopharm	2mg	\$234	\$95.16 -59%				colorectal cancer, 5-FU intolerable
Alecensa <sup>®</sup> (alectinib)	Roche			Undisclosed				NSCLC, ALK+
Lynparza <sup>®</sup> (olaparib)	AstraZeneca			Undisclosed				Epithelial ovarian, fallopian tube, or peritoneal cancer
Airuini <sup>®</sup> (pyrotinib)	Hengrui			Undisclosed				Breast cancer, HER2+, 2L
Perjeta <sup>®</sup> (pertuzumab)	Roche			Undisclosed				Breast cancer, HER2+, neoadjuvant
Jakafi <sup>®</sup> (ruxolitinib)	Incyte / Novartis			Undisclosed				PMF, PPV-MF, PET-MF

			Unit Pricing	(US\$) <sup>[3]</sup>		Approximate Monthly Pi	ricing (US\$)	[3]	
Brand (generic)	Company	Dosage	'17 NRDL	'19 NRDL	$\Delta$ %	Dosage	'17 NRDL	'19 NRDL	Indication coverage
AiTan® (apatinib)	Hengrui	425mg <sup>[2]</sup>	\$29.03	\$24.56	-15%	850mg QD.	\$1,740	\$1,470	3L gastric adenocarcinoma or GEJ with adenocarcinoma.
EnDu® (rh-endostatin)	Simcere	15mg	\$89.62	\$69.70	-22%	7.5mg/m² iv QD 2wks/1wk-off.	\$1,430	\$1,120	Late-stage NSCLC.
Epidaza® (chidamide)	Chipscreen	5mg	\$54.77	\$48.79	-11%	30mg QD, 2x per wk.	\$2,820	\$2,510	2L+ Recurring or refractory peripheral T-cell lymph. (PTCL).
Avastin® (bevacizumab)	Roche			Undisclosed					Late-stage meta. CRC or advanced non-squamous NSCLC.
TheraCIM®[4] (nimotuzumab)	Biotech			Undisclosed					Combo with RT for EGFR+ III/IV nasopharyngeal carcinoma.
Tarceva® (erlotinib)	Roche			Undisclosed					Advanced NSCLC with limited EGFR gene mutation.
Herceptin® (trastuzumab)	Roche			Undisclosed					Breast: Her2+; Her2+ meta. Her2+ late-stage meta. gastric.
Afinitor® (everolimus)	Novartis			Undisclosed					RCC after sunitinib or sorafenib. Pancreatic NETs. TSRA.
Nexavar® (sorafenib)	Bayer			Undisclosed	l				RCC or HCC. meta. diff. thyroid after radio-iodine therapy.





HUTCHISON CHINA MEDITECH

Thank you