







# CSTONE PHARMACEUTICALS (2616.HK) 2019 ANNUAL RESULTS PRESENTATION

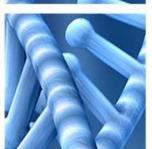














March 27, 2020

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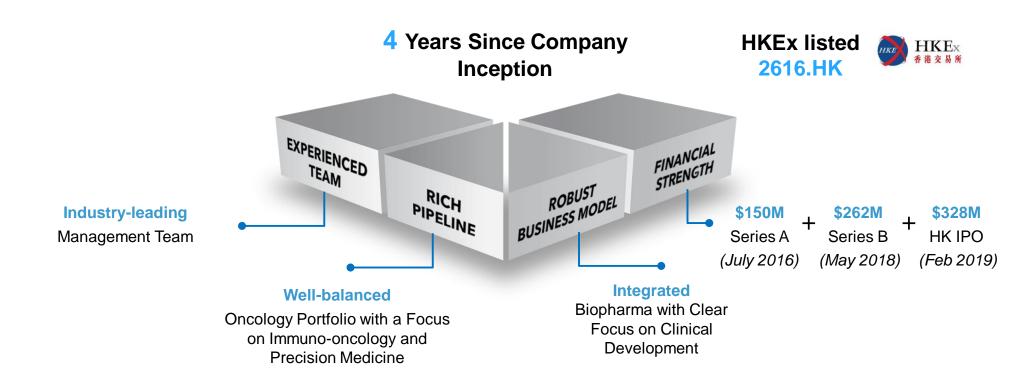
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### To Become Globally Recognized as the Leading Chinese Biopharma



### Industry leading management team with proven track record and complementary expertise





Frank Jiang, MD, PhD Chairman, Chief Executive Officer







Shirley Zhao, MD, MBA Greater China GM. Head of Commercial





Jason Yang, MD, PhD Chief Medical Officer







Richard Yeh, MBA Chief Financial Officer







Bing Yuan, PhD, MBA Chief Strategy and **Business Officer** 







Jon Wang, PhD Chief Scientific Officer



Archie Tse. MD. PhD Chief Translational Medicine Officer









Jingrong Li, PhD SVP, Product Development & Manufacturing







Sanhu Wang, MD SVP, Government Affairs









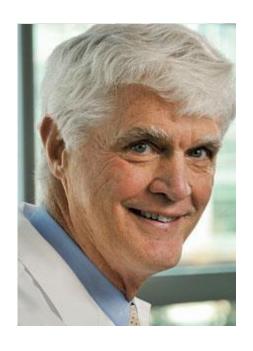


**Yinghua Zhang** VP, Operations



# Distinguished world-class scientific advisory board with deep oncology and IO expertise











Paul Bunn MD

Former ASCO President 2002-2003 Distinguished Professor, University of Colorado

Elizabeth Jaffee MD

Former AACR President 2018-2019 Professor of Oncology, Johns Hopkins University

Weiping Zou MD, PhD

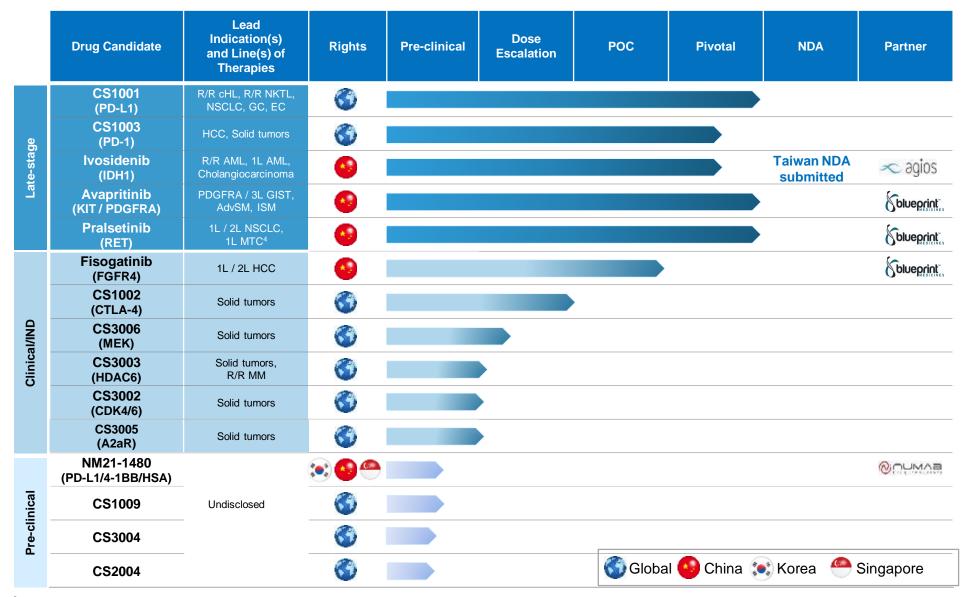
Chair, AACR Cancer Immunology Charles B.de Nancrede Professor, University of Michigan

Richard Finn MD

Former International
Liver Cancer
Association President
Clinical Professor,
UCLA

# Well-balanced oncology portfolio with a focus on immuno-oncology and precision medicine





Source: Company

Note: Assets status denote progress in the region noted in the column titled "Rights". AML= Acute Myeloid Leukemia, AdvSM = Advanced Systemic Mastocytosis, cHL= Classical Hodgkin's Lymphoma, GIST = Gastrointestinal Stromal Tumor, HCC = Hepatocellular Carcinoma, ISM = Indolent Systemic Mastocytosis,

NKTL = Natural KILLER/T Cell Lymphoma, NSCLC = Non-small Cell Lung Cancer, MTC = Medullary Thyroid Cancer, R/R = Relapsed or Refractory, SM = Systemic Mastocytosis, MM = Multiple Myeloma.

# Focus on China's largest indications, covering 55%+ of total cancer incidences



| Cancer type                         | Lung Cancer                                | Colorectal<br>Cancer           | Gastric Cancer                    | Liver Cancer                      | Esophagus<br>Cancer            |
|-------------------------------------|--|--------------------------------|-----------------------------------|-----------------------------------|--------------------------------|
| New cases<br>(2018)                 | 774,323                                    | 516,859                        | 456,124                           | 392,868                           | 307,359                        |
| 5-year prevalence<br>(2018)         | 716,411                                    | 1,237,145                      | 603,851                           | 296,780                           | 284,163                        |
|                                     | PD-L1 Mono<br>Stage III NSCLC              | PD-L1+Regorafenib Advanced CRC | PD-L1 + Chemo<br>Advanced GC/GEJ  | PD-1 + VEGFRi<br>Advanced HCC     | PD-L1 + Chemo<br>Advanced ESCC |
| Ongoing and planned clinical trials | PD-L1 + Chemo<br>Stage IV NSCLC            | PD-1+Regorafenib Advanced CRC  | PD-L1+Regorafenib Advanced GC/GEJ | Fisogatinib<br>FGF19+ HCC         |                                |
| registrational exploratory          | Pralsetinib<br>RETm 1L NSCLC<br>& 2L NSCLC |                                | PD-1+Regorafenib Advanced GC/GEJ  | PD-L1 + Fisogatinib<br>FGF19+ HCC |                                |

# Sizable portfolio anchored around 3 IO backbone agents to drive differentiated combo strategy



3
IO backbone agents

Only company in China owns clinical stage PD-L1, PD-1 and CTLA-4 assets in the pipeline

10 in-house developed derisked assets plus5 in-licensed FIC/BIC assets

potential 2<sup>nd</sup> generation of PD-(L)1

PD-L1x4-1BB provides more flexible combo and potential better efficacy

### **De-risked Combo**

PD-L1 + chemo/radiation

PD-(L)1 + Regorafenib

PD-1 + CS1002 (CTLA-4)

PD-L1 + Donafenib

### Novel Combo Unique to CStone

PD-L1 + Fisogatinib (FGFR4)

PD-(L)1 + CS3002 (CDK4/6)

PD-1 + Ivosidenib (IDH1)

Potentially more...

### Multi-specific/Multifunctional

NM21-1480 (PD-L1 x 4-1BB)

Potentially more...

11 combo trials, including 5 registrational trials

# Clinical Development Engine: Strong in-house team led by experienced leaders and supported by global CROs





Frank Jiang, MD, PhD Chairman and CEO

- Former Head of APAC R&D for Sanofi
- Led a 21,000 patient mega-trial
- Led 79 clinical trials and 30 NDAs within five years



Jason Yang, MD, PhD CMO

- Former SVP and Head of Clin Dev for Beigene, led development of PD-1, BTK, PARP and RAF dimer inhibitors
- Led 40+ global and China trials

Responsible for late stage clinical development and regulatory affairs



Archie Tse, MD, PhD CTMO

- Former Executive Director of Early Clin Dev at MSD (US)
- Led 30+ FIH oncology trials
- Led 20+ I/O combination trials

Responsible for early stage clinical development and diagnostics/biomarkers

Clinical Development & PV (1)



Biometrics & Medical Writing

Quality Assurance Clinical Operations Molecular Diagnostics

Translational Medicine & Biomarker Clinical Pharmacology

Early Development

Strong in-house team with  $\sim 170$  clinical staff, representing  $\sim 60\%$  of total employees, of which  $\sim 75\%$  hold advanced degrees (2) and  $\sim 80\%$  have clinical development experience at MNCs



PAREXEL.





Keep clinical strategy planning & development oversight in-house, while outsourcing day-to-day execution to global CROs to ensure optimal balance between efficiency and scalability

<sup>(1)</sup> Includes GI cancer, lung cancer, hematology & other solid tumors, and pharmacovigilance

### Significant clinical progress - overview 28 trials including 5 assets in 13 registrational trials today



### CS1001 (PD-L1)

- 6 registrational trials in China
  - Stage III NSCLC, stage IV NSCLC, GC, ESCC, NKTL and cHL

### CS1003 (PD-1)

- 1 registrational trial
  - HCC (global)

### Ivosidenib (IDH1)

- 2 registrational trials
  - IDH1m AML, R/R AML

### Avapritinib (KIT&PDGFRA)

- 2 registrational trials
  - PDGFRA exon 18 GIST, 3L GIST

### Pralsetinib (RET)

- 2 registrational trials
  - 2L NSCLC, 1L MTC

### Significant clinical progress – CS1001 (PD-L1) (1/5)



#### **Asset overview**

### Unique design

- Fully-human, full length lgG4 derived from Ligand's OmniRat® platform minimal possibility of generating ADA;
- The only PD-L1 antibody that naturally lacks of ADCC/CDC activity better safety and avoid unwanted attack of T cells;
- Retains ADCP activity that potentially induces direct tumor killing and macrophages and enhances tumor antigen presentation for long-term anti-tumor immunity – more efficacious in certain indications like NKTL

### Prominent safety profile

- Early phase studies demonstrated that CS1001 was safe & well tolerated
  - No DLT¹ from 3 mg/kg to 40 mg/kg, MTD² not reached
  - No infusion reactions; low ADA<sup>3</sup> rate
  - Low frequency of severe irAEs

### Best-in-class potential

- POC data of CS1001 showed potential of best-in-class PD-L1
  - Encouraging anti-tumor activities observed in phase la dose-escalation study, multiple phase lb cohorts and phase II studies
  - In particular, promising data in ESCC and in NKTL

# Significant development progress

- >1,200 patients dosed, with 6 registration trials ongoing, including 2 pivotal Ph II studies and 4 Ph III studies
- Strategically targeting China prevalent cancers including S3 and S4 lung cancer, GC and EC

<sup>\*</sup> as of Jan 2, 2020

<sup>1.</sup> DLT: dose limiting toxicity

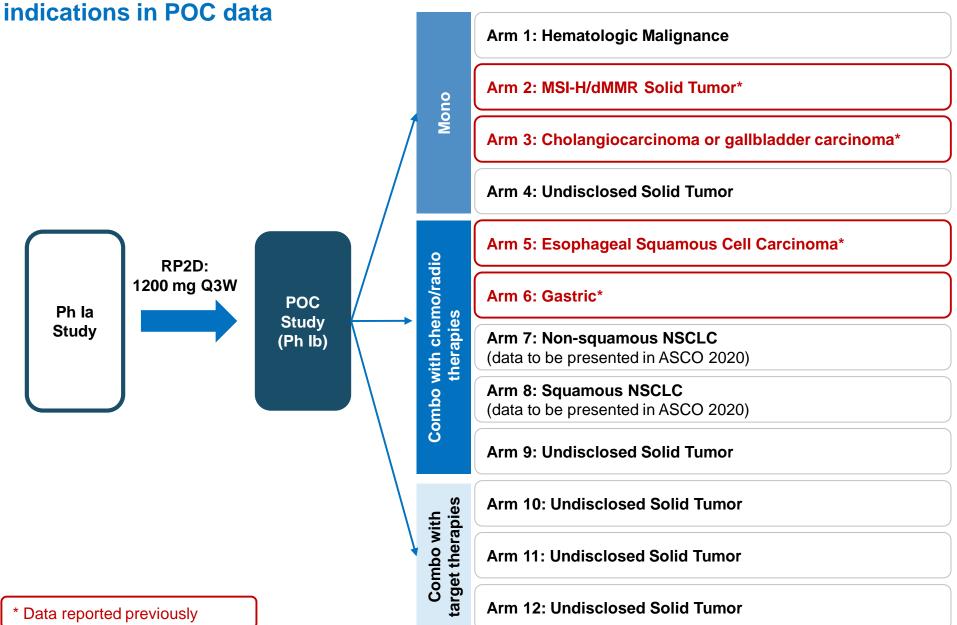
<sup>2.</sup> MTD: maximum tolerated dose

<sup>3.</sup> ADA: anti-drug antibodies

### Significant clinical progress – CS1001 (PD-L1) (2/5)

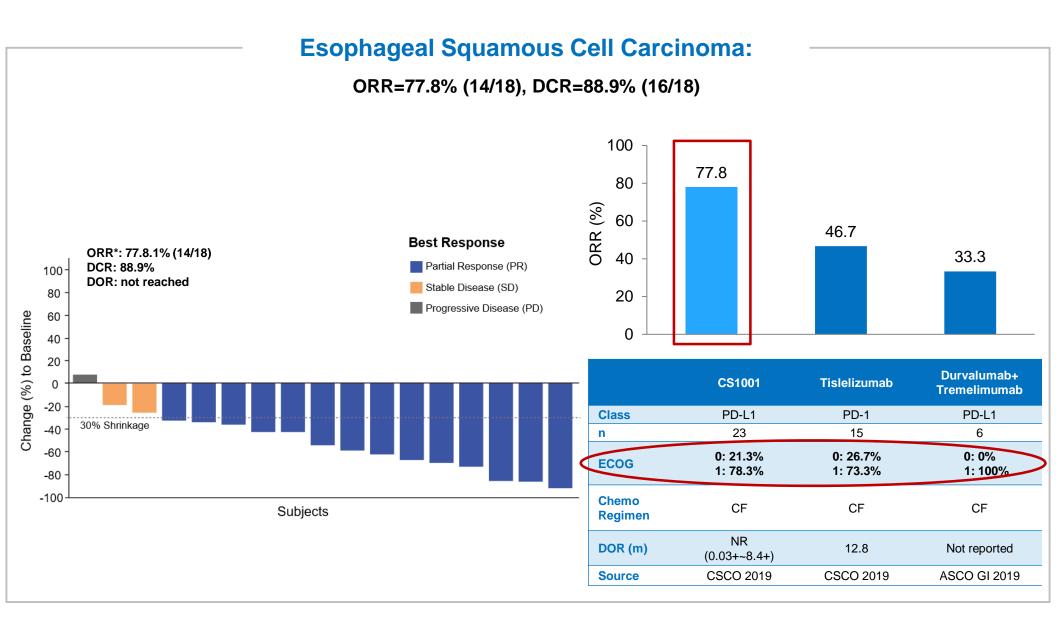


Phase la & lb study data: best-in-class potential in multiple



## Significant clinical progress – CS1001 (PD-L1) (3/5) Phase Ib study data: CS1001 + CF (Cisplatin + 5-FU) in 1L ESCC





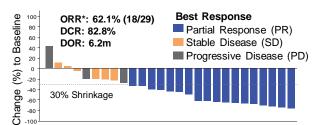
### Significant clinical progress – CS1001 (PD-L1) (4/5) Phase Ib study data: other cohorts



CS1001 + XELOX (Capecitabine + Oxaliplatin) in 1L GC/GEJ (Gastric or **Gastroesophageal Junction** Adenocarcinoma)

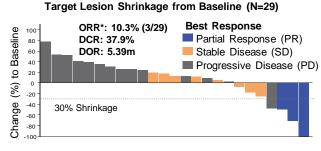
#### CS1001 (PD-L1) as monotherapy in CC/GBC (Cholangiocarcinoma or **Gallbladder Carcinoma)**

#### CS1001 (PD-L1) as monotherapy in MSI-H/dMMR Cancer

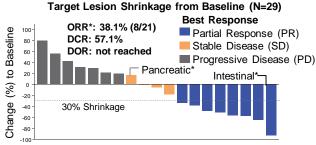


Target Lesion Shrinkage from Baseline (N=29)

\* 15 confirm PR; 3 PR to be confirmed as of data cut off on 1 July 2019

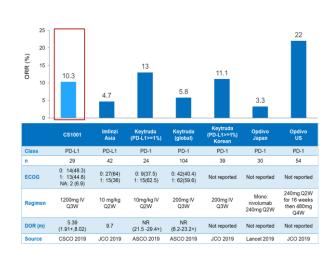


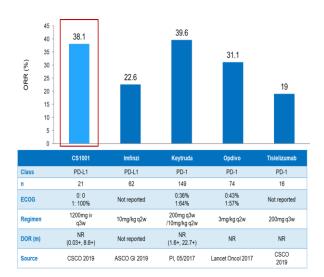
\* 2 confirm PR; 1 PR to be unconfirmed as of data cut-off on 1 July 2019



\*\* Unless specified, all patients were Colorectal Cancer







30% Shrinkage

<sup>\*</sup> ORR of Cisplatin + 5-FU or Capecitable was 37.3%

## Significant clinical progress – CS1001 (PD-L1) (5/5) Phase II study data: CS1001 as monotherapy in rr-ENKTL



#### Preliminary efficacy data

CS1001 demonstrated promising antitumor activity with a high CR rate and durable response in rr-ENKTL patients

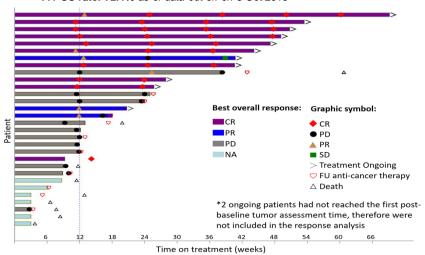
- Among the 22 efficacy-evaluable patients, the investigator-assessed ORR was 40.9%
- 7 (31.8%) patients achieved complete response
- The duration of response (DOR) ranged from 0.03+ to 8.61+ months, and the median DOR was not reached
- 8 additional pts reached response assessment time point, the updated data will be reported as poster presentation at the 2019 ASH conference

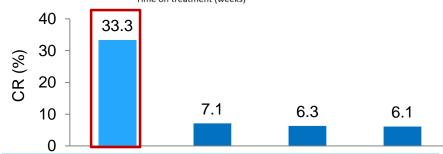
### CR is more clinically meaningful for r/r ENKTL

- Patients with CR have long duration of response while patients with PR generally progress quickly [1,2].
- High CR rate translates to potential allogeneic HSCT and curation of the disease [3].

#### Duration of treatment, Best response, Duration of response (N=30)

ORR = 43.3% (13/30), CR = 33.3.% (10/30), DOR not reached 1Yr OS rate: 72.4% as of data cut-off on 8 Oct 2019





| CS1001               | Sintilimab   | Chida<br>(Approved in rr-P  | mide<br>TCL, China, 2014)  |
|----------------------|--|---|--|
| PD-L1                | PD-1   | HDA   | AC   |
| CS1001-201           | ORIENT-4   | Registration Study  | Real World Study   |
| 30                   | 28   | 16  | 33   |
| <b>33.3%</b> (10/30) | 7.1% (2/28)  | 6.3% (1/16)   | 6.1% (2/33)  |
| NR<br>(0.03+~8.61+)  | 4.1<br>(0+,4.2+)                                   | UNK   | UNK  |
| ASH 2019             | ASCO 2019  | Ann Oncol, 2015 <sup>[4]</sup>  | J Hematol Oncol,<br>2017 <sup>[5]</sup>  |
|                      | PD-L1 CS1001-201 30 33.3% (10/30) NR (0.03+~8.61+) | PD-L1 PD-1  CS1001-201 ORIENT-4  30 28  33.3% (10/30) 7.1% (2/28)  NR 4.1 (0.03+~8.61+) (0+,4.2+) | CS1001 Sintilimab (Approved in rr-P' PD-L1 PD-1 HD/A CS1001-201 ORIENT-4 Registration Study 30 28 16 33.3% (10/30) 7.1% (2/28) 6.3% (1/16)  NR 4.1 UNK |

### Strategic value

### Significant clinical progress – CS1003 (PD-1) and CS1002 (CTLA-4)

Two Additional I/O Backbones: preliminary data and development strategy



#### **CS1003**

#### **CS1002**

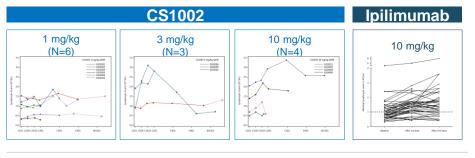
- Humanized IgG4 anti-PD-1 mAb
- Recognize both human & murine PD-1 with unique advantage to evaluate efficacy in syngeneic mouse models, esp. for testing combinations with small molecules
- A full-length, fully human IgG1 mAb against CTLA4
- Amino acid sequence identical to ipilimumab (Yervoy)
- Bridging Ph1 conducted in China showed that CS1003 monotherapy was safe and tolerable at 60mg and 200mg Q3W: no DLT or MTD was observed (N=19)
- Dose proportional increase in systemic exposure to CS1003
- Preliminary anti-tumor activity of CS1003 observed in multiple tumor types (PR 3/16 (18.8%))

- CS1002 monotherapy was well tolerated up to 10 mg/kg Q3W, with no DLT and no MTD reached (N=13)
- CS1002 demonstrated dose-proportional PK; increase in absolute lymphocyte count (ALC) observed indicating target engagement
- Overall clinical profile is consistent with that of ipilimumab

#### Preliminary efficacy in multiple tumor types

### Best Change in Target Lesion from Baseline (%) 25.0% 37.5% CS1003 200 mg CS1003 60 mg 10

### CS1002 induced early ALC increase, similarly to Ipilimumab



- One of 3 I/O backbones with current safety and efficacy data supporting further development
- Initiated combo study with CS1002, and combo study with lenvatinib in Ph3 trial for 1L HCC
- Potentially become another outstanding CTLA-4 inhibitor after Ipilimumab, which has not been launched in China
- One of 3 I/O backbones to enable flexible combo strategy, including chemo-free I/O-I/O combo with CS1003

DLT: dose-limiting toxicity; MTD: maximum tolerated dose; Q3W: once every 3 weeks; PK: pharmacokinetics; ADA: anti-drug antibody; PR: partial response; VEGF: vascular endothelial growth factor; TKI: tyrosine kinase inhibitor; HCC: hepatocellular carcinoma

# Significant clinical progress – ivosidenib (CS3010) Global and China development and regulatory status



### Global

| Partner | Drug Candidate     | Target | Indications                         | Pivotal / Registrational Trial<br>Patient Enrollment | NDA<br>Submission | NDA Approval |
|---------|--------------------|--------|-------------------------------------|--|-------------------|--------------|
|         |                    |        | R/R AML                             |  |                   | <b>✓</b>     |
|         | ~ agios Ivosidenib | IDH1   | IC-Ineligible 1L AML monotherapy    |  |                   | <b>~</b>     |
| ogios   |                    |        | IC-Ineligible 1L AML combo with AZA | <b>✓</b>   |                   |              |
|         |                    |        | 2/3L Cholangiocarcinoma monotherapy | <b>✓</b>   |                   |              |

✓ Achieved

### **Greater China**

| Partner | Drug<br>Candidate   | Indications                               | Region | Mono<br>/Combo | Study Initiation        | Patient Enrollment |   |           |
|---------|---------------------|---|--------|----------------|-------------------------|--------------------|---|-----------|
|         |                     | IDH1m R/R AML                             | Taiwan | Mono           | Registration with US ND | DA data            | 5 | submitted |
| → agios | lvosidenib (CS3010) | IC-Ineligible 1L<br>AML<br>combo with AZA | China  | Combo          | Joining global study    |                    |   |           |
|         |                     | IDH1m R/R AML                             | China  | Mono           | Bridging study          |                    |   |           |

### TIBSOVO®: global first-in-class IDH1 inhibitor



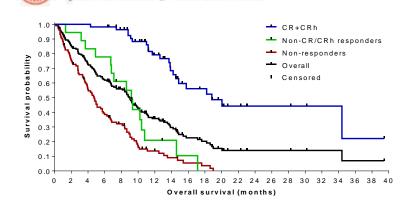
### No immediate competitor in China; significant indication expansion potential

In Partnership With





The NEW ENGLAND JOURNAL of MEDICINE

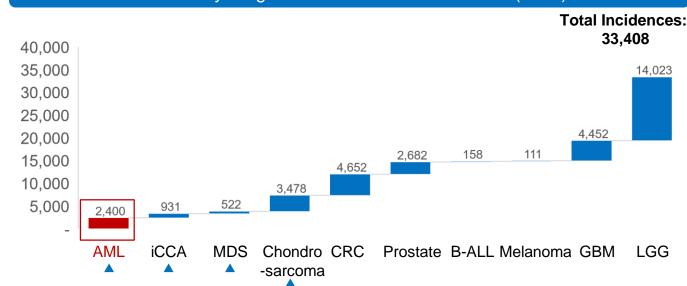


U.S. FOOD & DRUG ADMINISTRATION

- **Fast Track Review**
- 2X Breakthrough Therapy Designation
- **Priority Review**

### Total Newly Diagnosed Addressable Incidences (2018)

Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML



Source: Globocan 2018; CStone analysis

### Significant clinical progress – avapritinib (CS3007) Global and China development and regulatory status

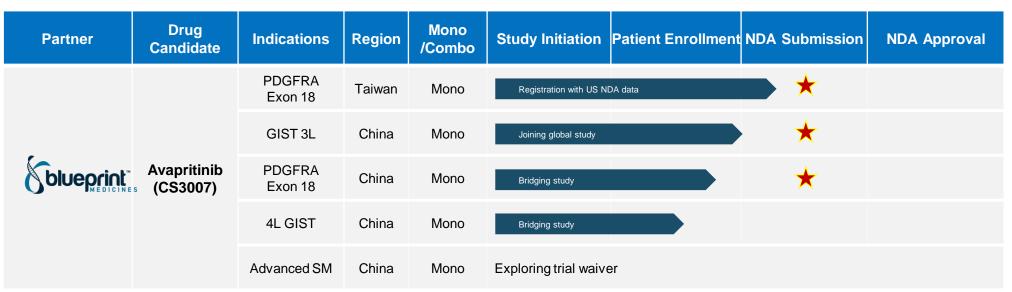


To be expected in 2020

#### **Global**

| Partne        | er          | Drug<br>Candidate | Target  | Indications            | Pivotal / Registrational Trial<br>Patient Target Enrollment | U.S. NDA<br>Submission | U.S. NDA<br>Approval |
|---------------|-------------|-------------------|---------|------------------------|---|------------------------|----------------------|
|               |             |                   |         | PDGFRA exon 18<br>GIST |   |                        | <b>~</b>             |
|               | Avapritinib | KIT &             | 4L GIST |                        | <b>~</b>  |                        |                      |
| <b>Splneb</b> | IEDICINES   | s (CS3007)        | PDGFRA  | 3L GIST                | <b>✓</b>  |                        |                      |
|               |             |                   |         | Advanced SM            | <b>✓</b> <sup>(1)</sup>                                     |                        |                      |

### **Greater China**



Note: AYVAKIT<sup>TM</sup> (avapritinib) is approved by the U.S. FDA for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations (1) Sufficient enrollment has been achieved to enable interim analysis supporting an H2 2020 filing, but the PATHFINDER trial is not fully enrolled



Achieved

### Avapritinib: global first-in-class PDGFRA/KIT inhibitor Targeted therapy with significant indication expansion potential



In Partnership With

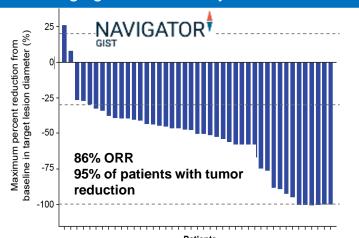


### U.S. FOOD & DRUG

- Fast Track Review
- 2X Breakthrough Therapy Designation
- Priority Review



### Encouraging Clinical Activity Shown in NAVIGATOR Registrational Phase 1 Study

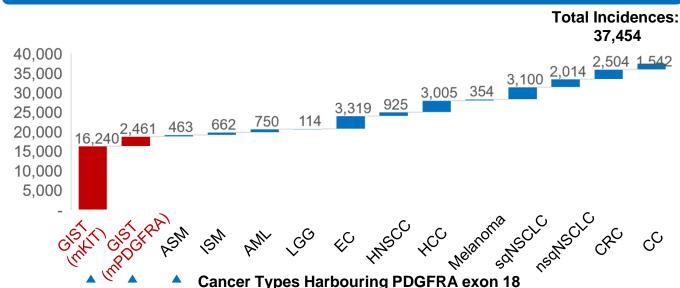


#### **Safety Summary**

- Most AEs were grade 1 or 2, with a higher incidence of commonly reported AEs in the 400 mg QD dose group compared with the 300 mg QD dose group.
- No treatment-related grade 5 AEs were reported.

Heinrich et al. 2020. Clinical Activity of Avapritinib in ≥4th Line (4L+) and PDGFRA Exon 18 Gastrointestinal Stromal Tumors (GIST). Poster presented at the Gastrointestinal Cancers Symposium, Jan 23 San Francisco, CA

### Total Newly Diagnosed Addressable Incidences in China (2018)



Source: Globocan 2018; CStone analysis; Avapritinib CTOS 2018 Presentation

**Global Patent Expiry** 

## Significant clinical progress – pralsetinib (CS3009) Global and China development and regulatory status



#### Global

| Partner                      | Drug<br>Candidate | Target | Indications | Pivotal / Registrational Trial<br>Patient Target Enrollment | U.S. NDA<br>Submission | U.S. NDA<br>Approval |
|------------------------------|-------------------|--------|-------------|---|------------------------|----------------------|
| hhuaciat"                    |                   | RET    | NSCLC*      | <b>✓</b> **   | <b>\</b>               |                      |
| <b>blueprint</b> Pralsetinib | KEI               | 2L MTC | <b>✓</b>    | <b>/</b>  |                        |                      |

✓ Achieved 
 To be expected in 2020

NDA submission expected in 2020

#### **Greater China**

| Partner            | Drug<br>Candidate    | Indications   | Region | Mono<br>/Combo | Study Initiation     | Patient Enrollment | NDA Submission | NDA Approval |
|--------------------|----------------------|---------------|--------|----------------|----------------------|--------------------|----------------|--------------|
|                    |                      | NSCLC 2L      | China  | Mono           | Joining global study |                    | *              |              |
| hlueociot"         | Pralsetinib (CS3009) | MTC 1L        | China  | Mono           | Joining global study |                    |                |              |
| <b>Solue print</b> |                      | NSCLC 1L      | China  | Mono           | Joining global study |                    |                |              |
|                    |                      | Basket cohort | China  | Mono           | Joining global study |                    |                |              |

Registrational Potential Study

Registrational Study

### Praisetinib: potentially first-in-class RET inhibitor Targeted therapy with significant indication expansion potential



In Partnership With







Overview

First China NDA Filing 20

First in Class molecule

# of Competitor(s) in Clinical Development

Lead over immediate competitor

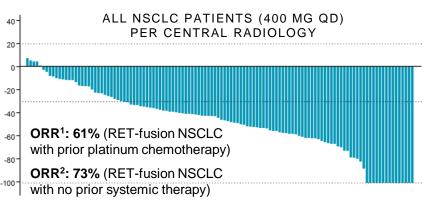
Global Patent Expiry 2036

vears

\*Eli Lilly's RETi currently not in China

### Broad and Durable Antitumor Activity in Patients with RET Fusion+ NSCLC

#### **ARROW**



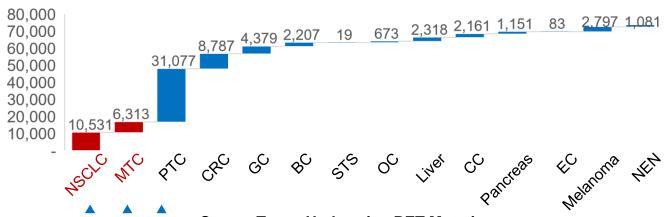
#### Safety Summary

- Safety results (N=354; 400 mg QD) were consistent with prior data; most reported AEs were grade 1 or 2"No treatment-related grade 5 AEs were reported.
- Overall, 4% of patients discontinued treatment due a treatment-related AE.

Top-line data from the Phase 1/2 ARROW trial in patients with RET fusion NSCLC. Data cutoff date: November 18, 2019. 1. Two responses pending confirmation. 2. All responses confirmed.

#### Total Newly Diagnosed Addressable Incidences in China (2018)

Total Incidences: 73.576



**Cancer Types Harbouring RET Mutation** 

▲ Active Clinical Programs

### Significant clinical progress on other clinical-stage assets





CS3005 (A2aR) Conducting a Ph I trial for solid tumors as monotherapy in Australia/China and plan to initiate a combo with CS1003 (PD-1) thereafter

CS3002 (CDK4/6) Conducting a Ph I trial for solid tumors as monotherapy in Australia/China and plan to initiate a combo with CS1003 (PD-1) thereafter

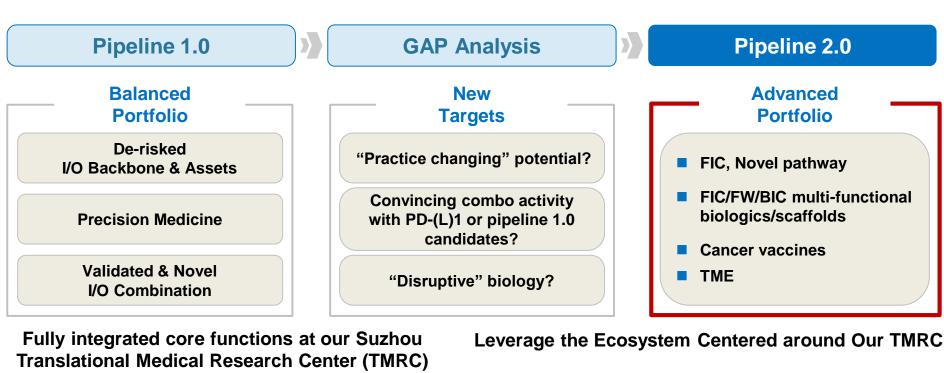
CS3003 (HDAC6) IND/CTA approvals received in China and Australia in March 2019 and April 2019 respectively

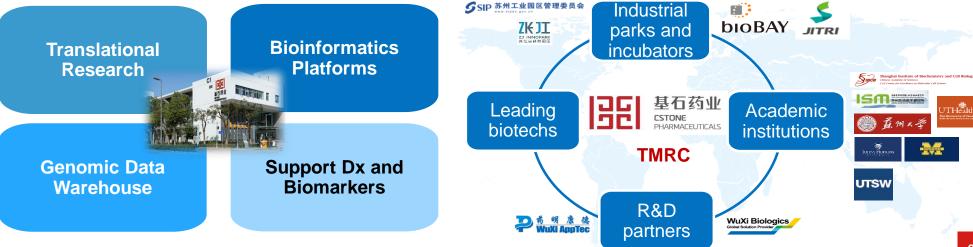
(MEK)

- Conducting a Ph I trial in Australia and expect to complete the dose escalation portion in 1Q20
- Conducting a Ph I trial in China and expect to complete the dose escalation portion in 1Q20

### CStone is driving pipeline 2.0 for sustained growth



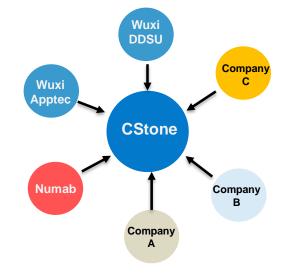




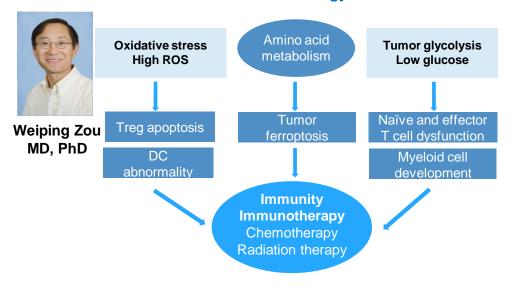
# Focus areas: novel biology, multi-functional biologics, cancer vaccines



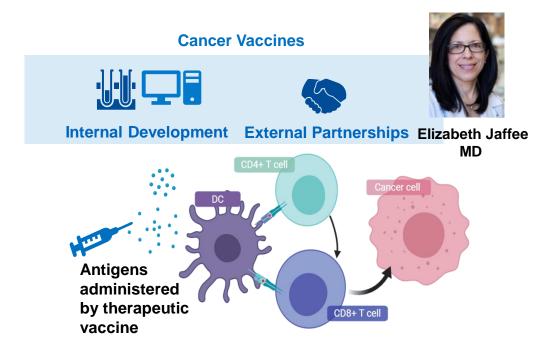
- CStone Internal Discovery Platform
  - "Hub & Spoke" models for internal projects
    - CStone names the targets; Internal PL&PM to run projects
    - Lead discovery & optimization done at CRO or platform companies until PCC, then bring back to CStone
  - Work with leading academic labs to identify lead candidates, then bring to CStone for development



#### **Novel Biology**



Targeting ferroptosis pathway may sensitize and improve immunotherapy efficacy



# ND021 (PD-L1x4-1BBxHSA) has the potential to be the BIC molecule as the next generation PD-(L)1 inhibitor



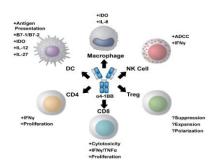
- Bridge new biology
- Improve therapeutic index & reduce unwanted toxic effects
- Expand combo options & improve administration convenience

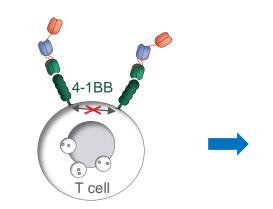
#### Six key features of ND021

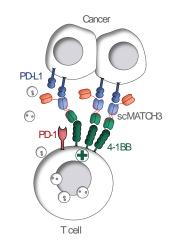
- Combination therapy in one molecule
   →expands combo options with SoC and other ICIs
- Monovalent 4-1BB binding remains inactive until PD-L1 engagement
   maximizes safety
- Ultra-high affinity (pM) to PD-L1→broadens PD-L1+ tumor types
- Standard affinity to 4-1BB (nM) →ensures effective activation
- HSA extends T1/2 & 100% effector null
   →enables convenient dosing & eliminated undesirable FcgR-mediated activation
- MW ~70kDa, only half of conventional mAb
   →leads to better tumor penetration &

→leads to better tumor penetration & efficacy

| 1 -9 | Irrelevant IgG (Palivizumab) | 2 | NM21-1186 (0.02 mg/occasion) | 3 | NM21-1186 (0.1 mg/occasion) | 4 | NM21-1186 (0.5 mg/occasion) | 5 | PD-L1 IgG + 4-1BB IgG | 6 | PDL1 IgG | 7 - B | Avelumab | 8 | Urelumab | NM21-1186 | NM21-1186 (0.5 mg/occasion) | 1 | NM21-1186 (0

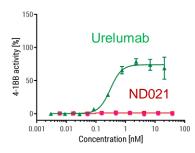




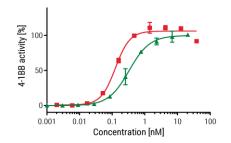


PD-L1 Negative

Time (days)



PD-L1 Positive



# Strategically partnering with global and domestic leading biopharmaceutical companies in past two years

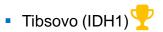




1

### 5 FIC/BIC Assets from 3 Global Partners







- Avapritinib (KIT & PDGFRA)
- Pralsetinib (RET)
- Fisogatinib (FGFR4)



ND021

2

### **3** Clinical Collaborations Deals Focused on IO Combo Therapy



CS1001 (PD-L1) + Donafenib



CS1001 (PD-L1) + Regorafenib



CS1001 (PD-L1)+ IMP4297



# Global collaboration deal with China focus to evaluate PD-L1 in combination with regorafenib in key indications











# Highlights

 First collaboration with a MNC pharma, one of the very few without PD-(L)1 – a vote of confidence in CStone and CS1001 (PD-L1)

# Strategic Value

- Further strengthens our core strategy in IO combination therapy
- A big step forward for CStone's global strategy in case of positive data

# **Progress Update**

In December 2019, the first patient was dosed in a Phase Ib trial of CS1001 in combination with regorafenib in Australia

### Regorafenib reported promising data with PD-1 in gastric cancer and colorectal cancer at ASCO 2019

| Indication              | Mono/Combo  | ORR             |
|-------------------------|-------------|-----------------|
| A 1                     | Pembro      | 13%¹            |
| Advanced GC             | Rego + Nivo | 44%²            |
|                         | Pembro      | 0%³             |
| pMMR/MSS                | Rego        | 2% <sup>4</sup> |
| CRC<br>(95% of<br>mCRC) | Atezo       | 2% <sup>4</sup> |
|                         | Atezo + MEK | 3% <sup>4</sup> |
|                         | Rego + Nivo | 33%²            |

Note: 1. KEYNOTE059; 2. 2019 ASCO data, All respondents were Microsatellite stable (MSS); 3. 2015 ASCO data; 4. IMBlaze370 pMMR = mismatch repair proficient

### We will focus on precision medicine in the near-term, followed by PD-(L)1 across China prevalent indications in the longer term



Near-term (2020~2021) Mid-term (2022~2025) Long-term (2026~) Expect ~13 potential approved products Across 20+ indications<sup>1</sup> Expect ~6 products Across 15 indications<sup>1</sup> PDGFRA GIST. **AYVAKIT** 3L GIST, 4L GIST avapritinib tablets 1L NSCLC, 2L NSCLC, Pralsetinib **Expect 4 products** PDGFRA GIST, 1L MTC **AYVAKIT** 3L GIST, 4L GIST TIBSOVO® Across 5 indications<sup>1</sup> r/r AML, NIC AML 1L NSCLC 1L, 2L NSCLC, Pralsetinib 1L MTC cHL OR NKTL. CS1001 S4 NSCLC, S3 NSCLC, (PD-L1) TIBSOVO° PDGFRA GIST. r/r AML, NIC AML **AYVAKIT** ESCC, GC 3L GIST cHL OR NKTL. CS1001 PD-1 **HCC** S4 NSCLC, S3 NSCLC, 2L NSCLC Pralsetinib (PD-L1) ESCC. GC Fisogatinib HCC r/r AML **HCC** TIBSOVO® PD-1 CTLA-4; CDK4/6; A2A; PD-L1/4-CS1001 HCC **Fisogatinib cHL OR NKTL** 1BB/HSA; CS1009, CS3004, CS2004

We are constantly filling our pipelines that fit with our pipeline 2.0 approach

(PD-L1)

# Shirley Zhao, a top commercial executive with 26 years experience to build and scale up commercial capabilities in Greater China



Greater China GM & Head of Commercial



Shirley Zhao MD, MBA



Former BMS China mainland and HK General Manager (GM), brought China's first PD-1 (OPDIVO) to the market and led a \$650M commercial operation



 Former Allergan China President, built China's commercial operation from \$10M to \$300M in 6 years, and become the 2<sup>nd</sup> biggest business in Allergan worldwide

• Former **Genzyme** China GM, successfully SANOFI GENZYME achieved registration milestones, and launched several rare disease drugs



10 years in Eli Lilly China as VP & Onco BU head,
 5 years in BMS, launched Taxol, Paraplatine,
 Gemzar, Alimta

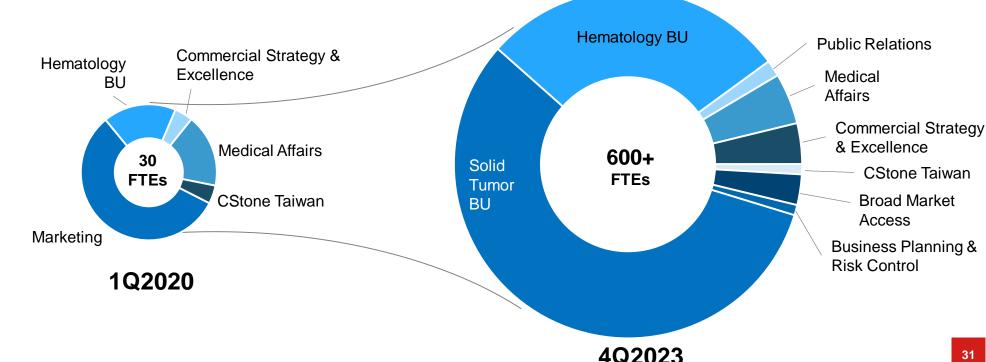


Former **OB/GYN** physician, received **MD** training in Clinical Medicine from Tongji University, and obtained **MBA** from University of Leicester

# Full-fledged commercial organization being scaled up for multiple launches in the next 2 years



Stage 3 2023+ Stage 2 2021-2023 Stage 1 2018-2021 Full launch of PD-L1 **Establish commercial** First wave of product and in-licensed assets launches outside China<sup>1</sup>, organization with core functions for Greater China across multiple major preferably with partner Scale up global commercial Focus on self-build indications Commercial model commercial model while Scale up Greater organization to support prelaunch planning and launch exploring potential value-driving **China** commercial strategic partnership presence Build and scale up commercial capabilities (Sales & Marketing; Access; Medical Affairs; Distribution; Launch & Commercial Excellence etc.) to support China and global launches, ramped up 18-24 months in advance of commercialization each launch

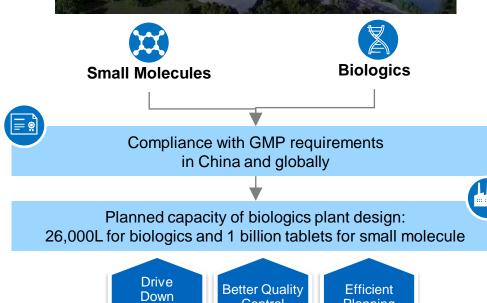


# Developing strong manufacturing capabilities for both biologics and small molecules



- In August, we entered into an agreement with Sungent (state-owned controlled by Suzhou Industrial Park) to build manufacturing facility
- Planned building area of approximately100,000 sqm
- Commissioned to a third party and is scheduled to break ground in 2020
- Capability: once completed, the complex will be equipped with integrated capabilities for R&D, Pilot Plant, and full commercial scale manufacturing
- Planned capacity: 26,000L for macromolecule biologics and 1 billion tablets and capsules for small molecule drugs
- Strategic partnership with Wuxi Biologics on clinical and commercial stage manufacturing





### **Financial summary in 2019**





### **Cash Balance**

- RMB2,726 million of cash, cash equivalents, and time deposits as of December 31, 2019 vs. RMB1,463 million as of December 31, 2018
- Cash position increased by RMB1,263 million mainly due to proceeds from our IPO in February 2019

### Sources of Cash

- **IPO proceeds**: HK\$2,394 million (post greenshoe)
- Other income: RMB84 million, mainly consists of interests income from bank deposits and time deposits

#### **Uses of Cash**

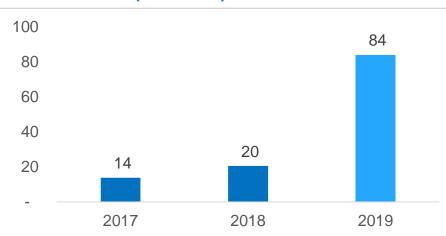
- Adjusted R&D expenses¹ (non-IFRS): RMB1,189 million
- Adjusted administrative expenses¹ (non-IFRS): RMB138 million
- Listing expenses: RMB18 million

### Financial summary in 2019 (continued)

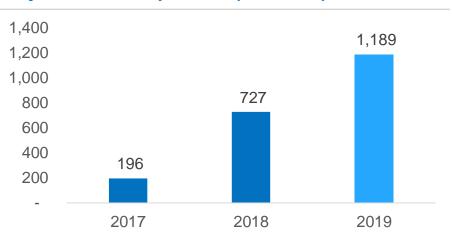


### Key income statement items

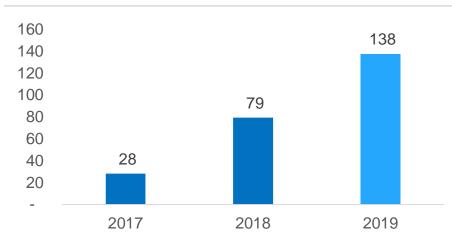
#### Other Income (RMB mm)



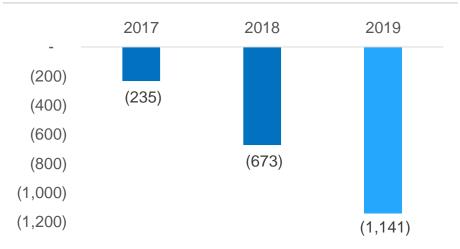
### Adjusted R&D Expenses<sup>1</sup> (RMB mm)



### Adjusted Administrative Expenses<sup>1</sup> (RMB mm)



### Adjusted Loss for the Period<sup>2</sup> (RMB mm)



<sup>1.</sup> Adjusted for share-based compensation

<sup>2.</sup> Adjusted for share-based compensation and loss from fair value changes of the conversion feature of preferred shares

### 2019 guidance

#### By the number

- 25+ clinical trials by year end
- Including 10+ registrational studies
- Approximately 10+ combination therapy trials

#### **NDA timeline**

■ Taiwan NDA planned for ivosidenib in 2019

#### **Data release**

- CS1001 (PD-L1)
- CS1003 (PD-1)
- CS3006 (MEK)

- Research: deliver 1-2 new molecule INDs each year
- Manufacturing: site selection in progress

### 2019 actual performance

#### By the number

- 28 clinical trials by year end
- Including 13 registrational studies
- 11 combination therapy trials

#### **NDA** timeline

Submitted ivosidenib in Taiwan

#### Data release

- CS1001 (PD-L1): Ph 1a published at ASCO, Ph lb and Ph II NKTL published at CSCO, ESMO, ASH
- CS1003 (PD-1): Ph la data published at CSCO
- CS1002 (CTLA-4): Ph la data published at CSCO
- Research: CS3002 (CDK4/6) and CS3005 (A2aR) entered clinical trials
- BD: licensed ND021 from Numab and reached clinical collaboration with Bayer
- Manufacturing: entered into an agreement to build manufacturing facility and global R&D headquarter in Suzhou
- Commercial: China GM Shirley Zhao on board

# Exciting year: 2020 will be a key inflection point for CStone, expecting the following major catalysts and goals



By year end 2020, 30+ clinical trials initiated, including 15 for registration

|  | 1 NDA<br>approval             | TIBSOVO<br>Ivosidenib   | ■ r/r AML, Taiwan  |
|--|-------------------------------|-------------------------|--|
|  |                               | PD-L1                   | ■ cHL (potentially NKTL), China  |
| Φ  | 5 NDA<br>submissions          | Avapritinib Pralsetinib | <ul> <li>PDGFRA exon 18 GIST, China</li> <li>3L GIST, China</li> <li>PDGFRA exon 18 GIST, Taiwan</li> </ul>  |
| <u>uli</u>   |                               | Praisetinib             | ■ 2L RET NSCLC, China  |
| Pipeline   |                               | PD-L1                   | <ul> <li>Stage IV NSCLC squamous and non-squamous Ib trial data at ASCO 2020</li> <li>Stage IV NSCLC registrational trial data by Q3 2020</li> <li>Stage III NSCLC registrational trial data by Q4 2020 / Q1 2021</li> </ul> |
|  | 7 Data readouts               | Avapritinib             | <ul> <li>3L GIST registrational trial data by Q2 2020</li> <li>GIST with PDGFRA exon 18 registrational trial data by Q2 2020</li> </ul>  |
|  |                               | Pralsetinib             | <ul> <li>2L NSCLC registrational trial data by Q3 2020</li> <li>1L MTC registrational trial data by Q4 2020</li> </ul>   |
| Commercial   |                               | Ivosidenib<br>Team      | <ul> <li>Product launch in Taiwan for r/r AML</li> <li>Build up commercial team to ~200 FTE</li> </ul>   |
| Busine   | Business Development Continue |                         | explore value creation partnership opportunities with domestic and multinational player  |
| Research Our partner Numab to submit NM21-1480 (ND021) U.S. IND next week (March 2020) |                               |                         | r Numab to submit NM21-1480 (ND021) U.S. IND next week (March 2020)  |



# Thank you!

