

# Ascentage Pharma Group

*Advancing Therapies That  
Restore Apoptosis*



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# Ascentage - Building a Global Biotech Company

Proprietary PPI science that offers first and best in class potential

## BREAKTHROUGH SCIENCE



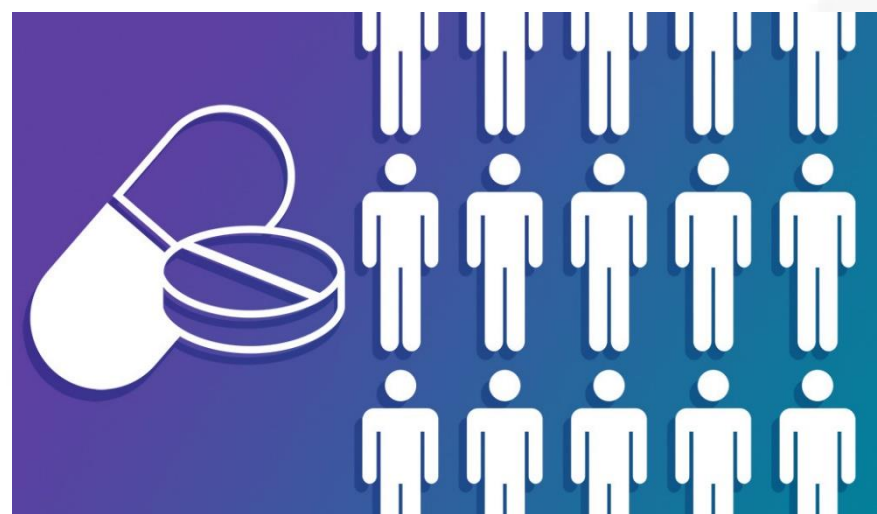
**80** ISSUED PATENTS  
**200+** PENDING APPLICATIONS  
**90+** PUBLICATIONS

## DEDICATED TEAM



**1** VISION: BUILDING A GLOBAL BIOTECH COMPANY  
**20+** YEARS' COMMITMENT OF 3 CO-FOUNDERS  
**400+** EMPLOYEES

## STRONG PIPELINES



**8** NOVEL COMPOUNDS  
**21** INDS  
**30+** CLINICAL TRIALS  
**10+** INDICATIONS

## GLOBAL OPERATION

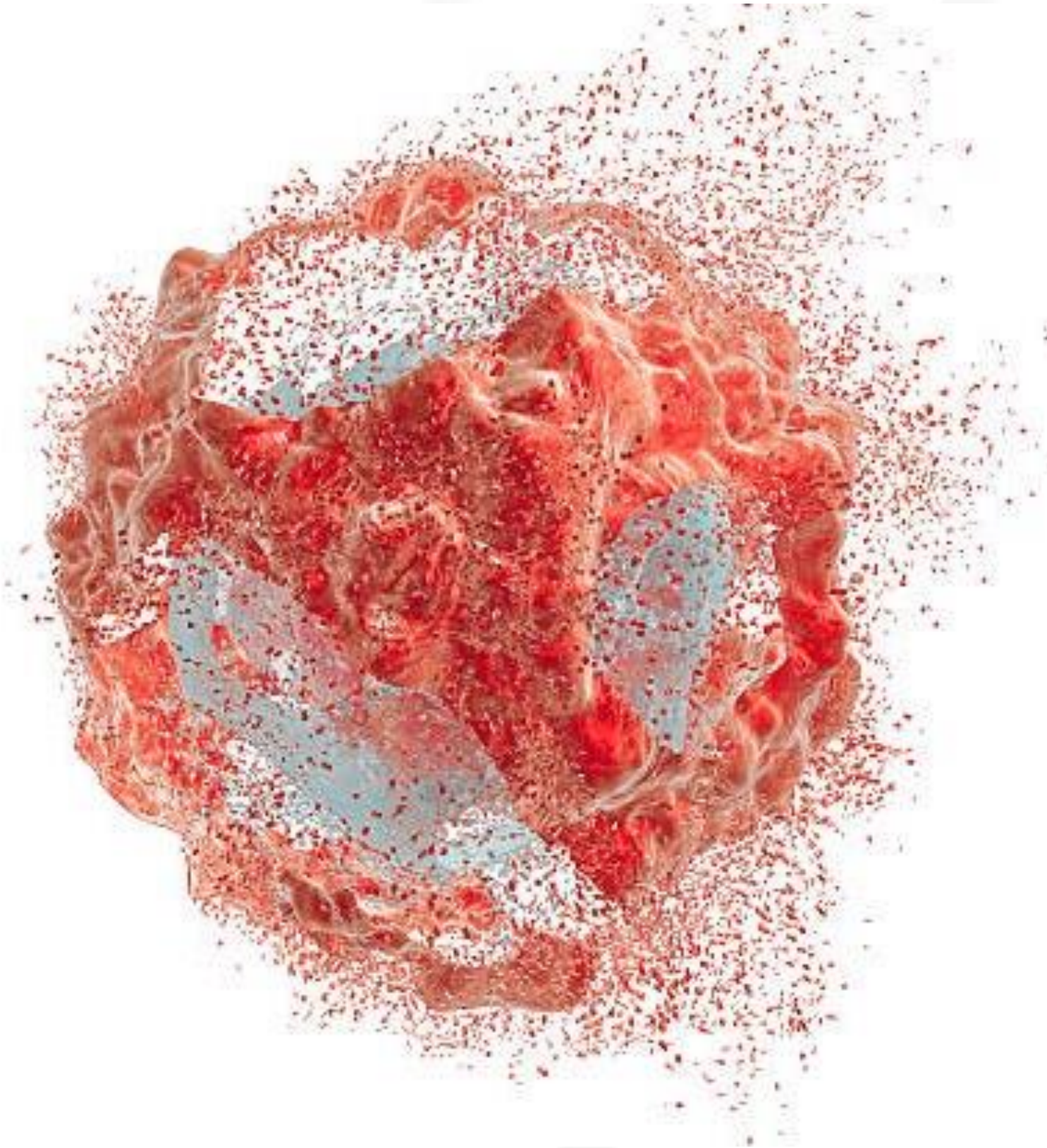


INTEGRATED ORGANIZATION IN  
**CHINA, UNITED STATES**  
AND **AUSTRALIA**



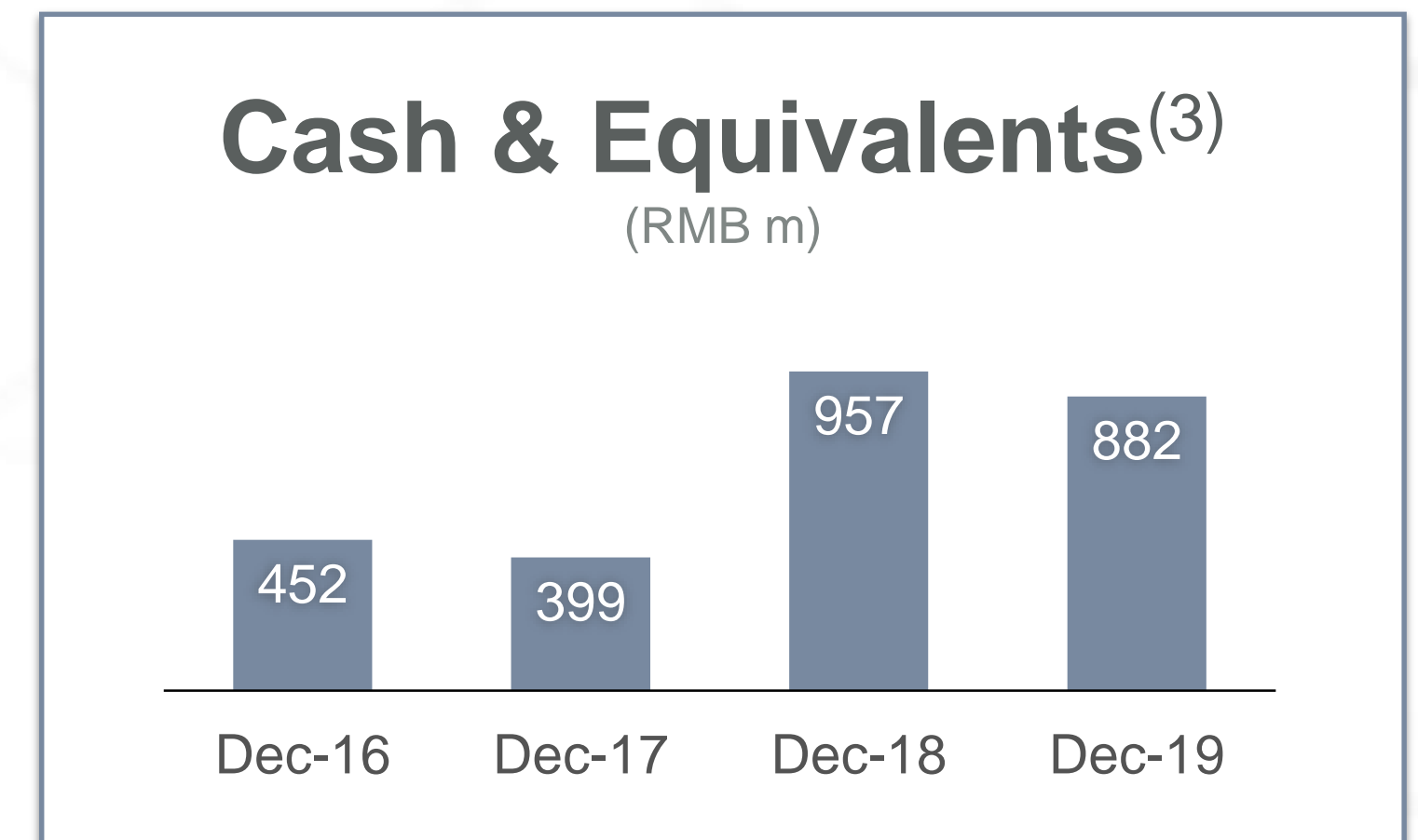
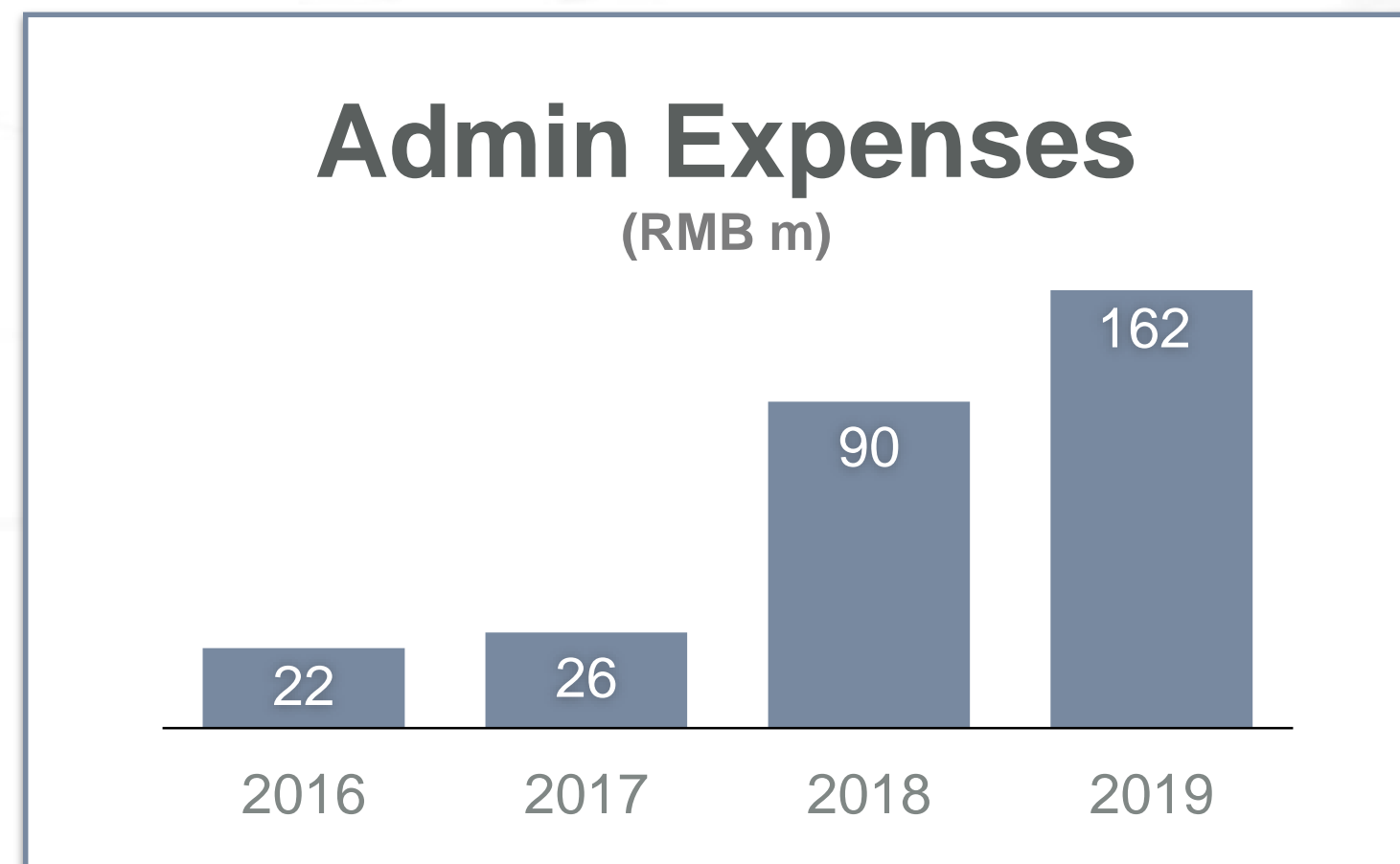
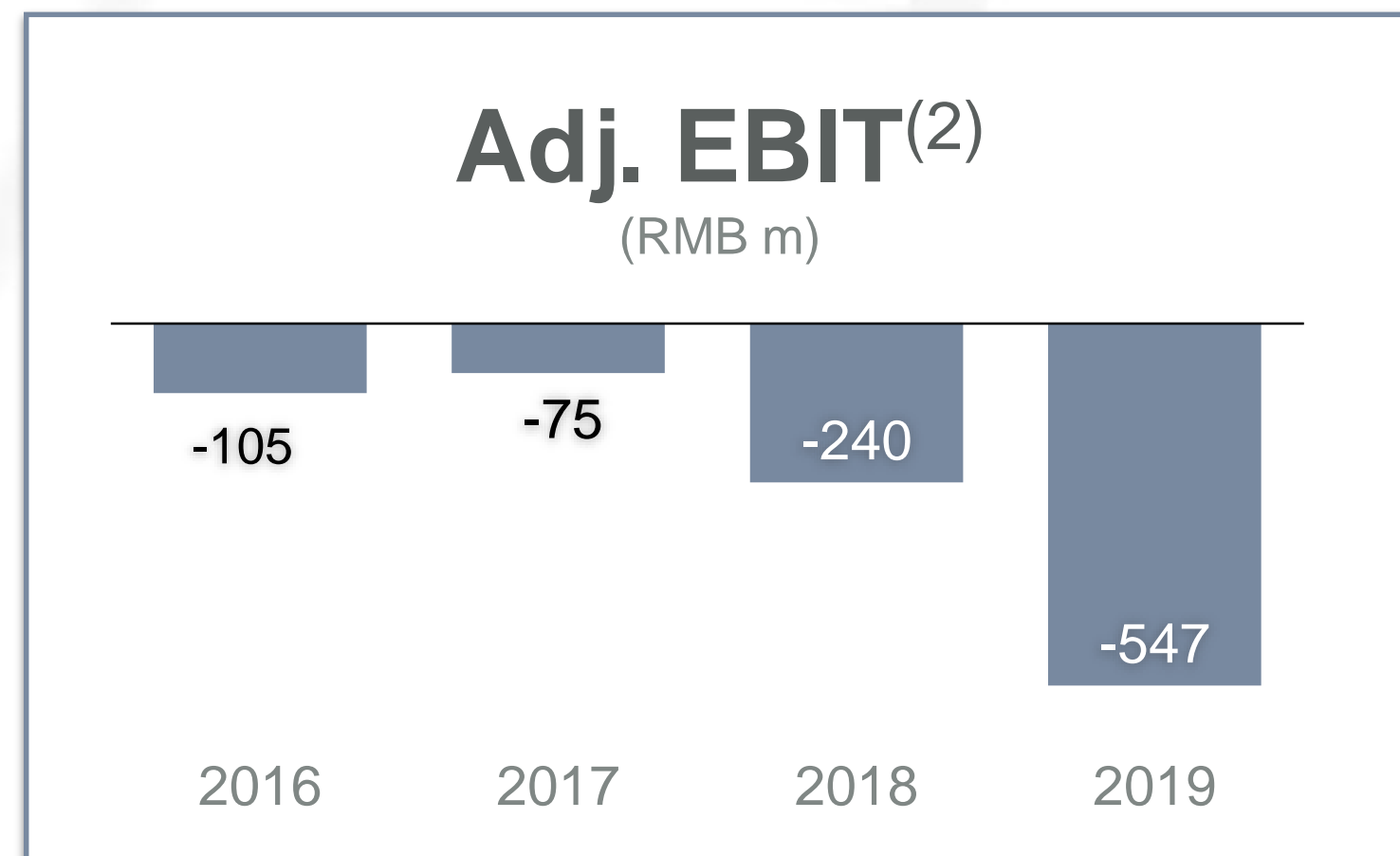
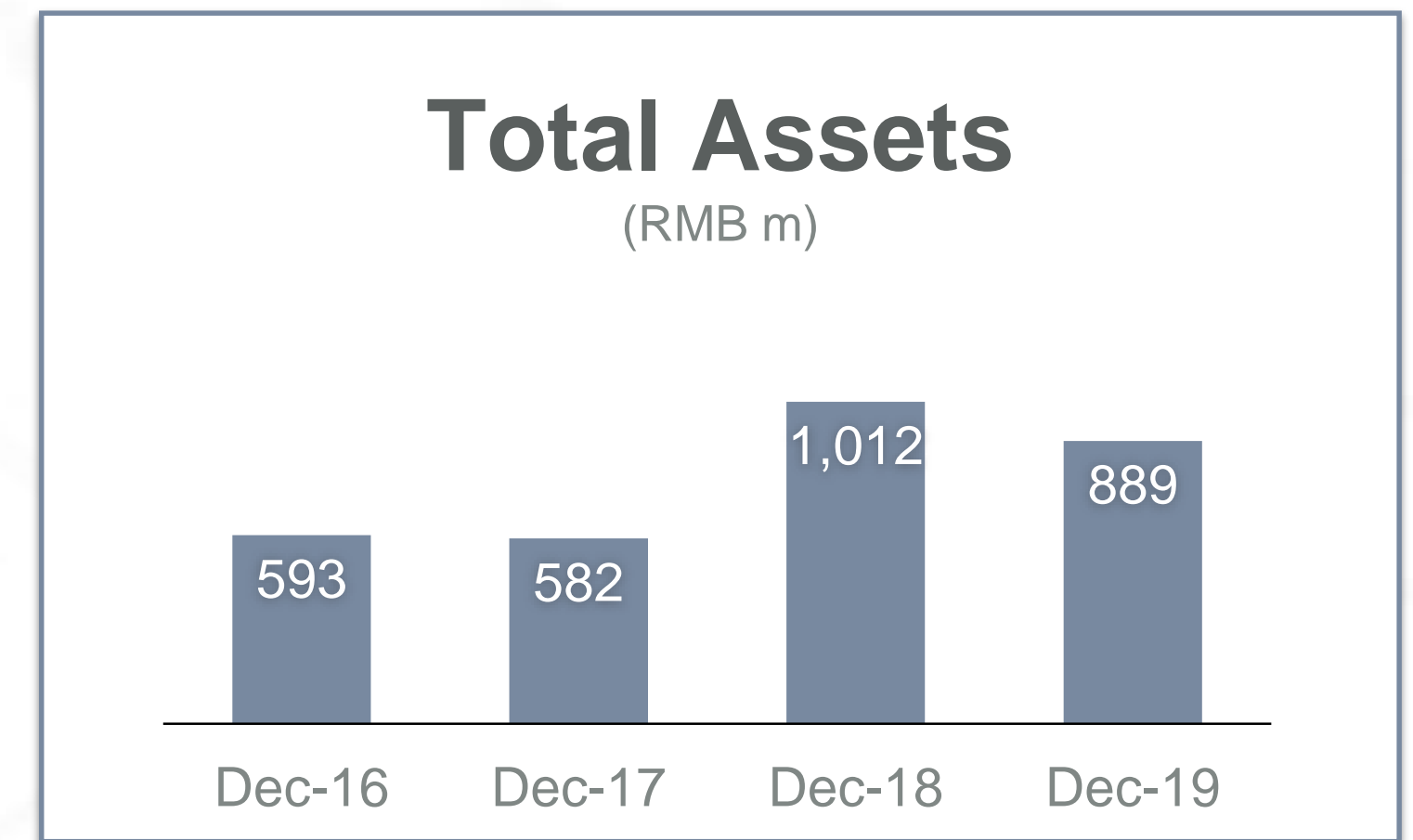
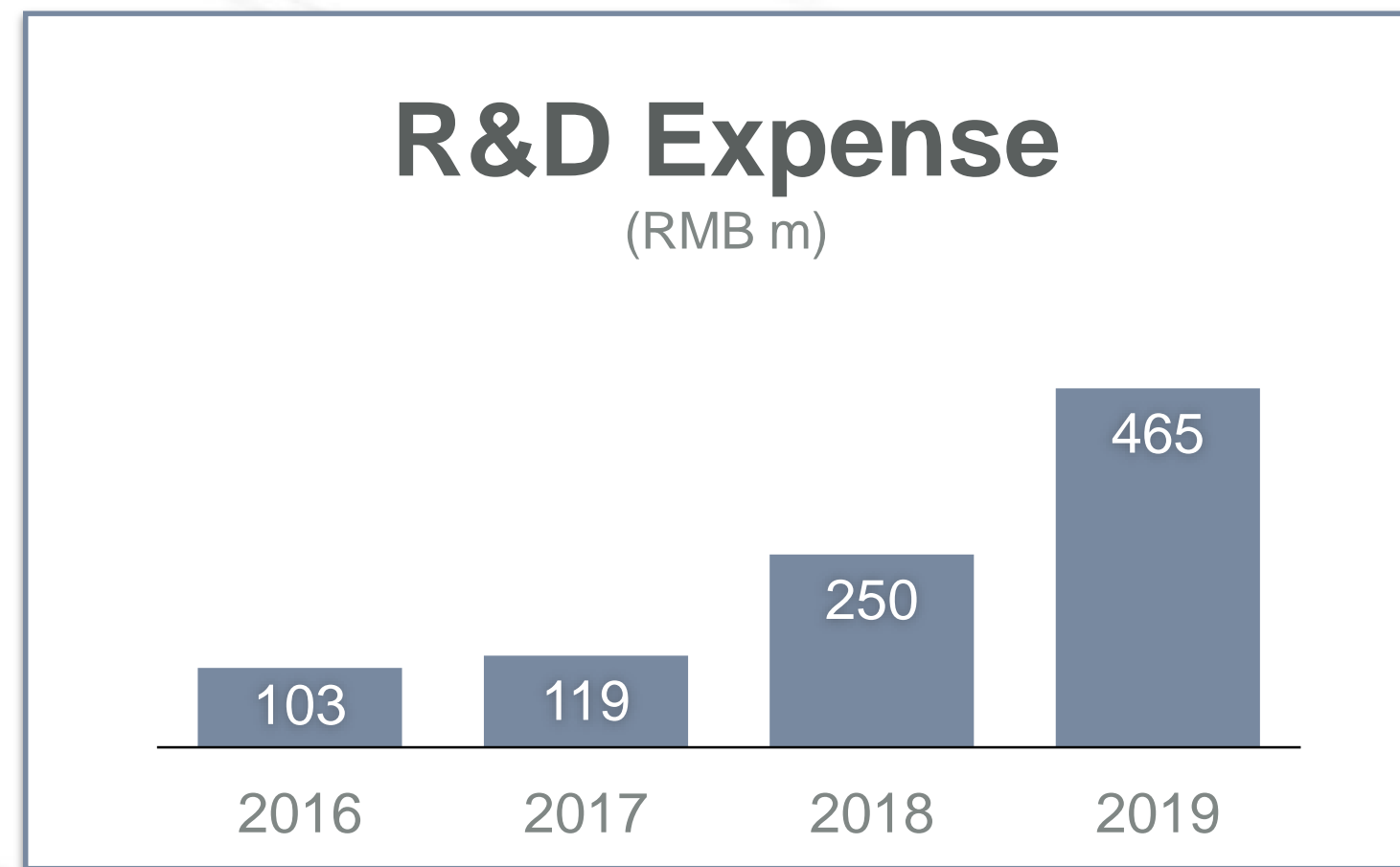
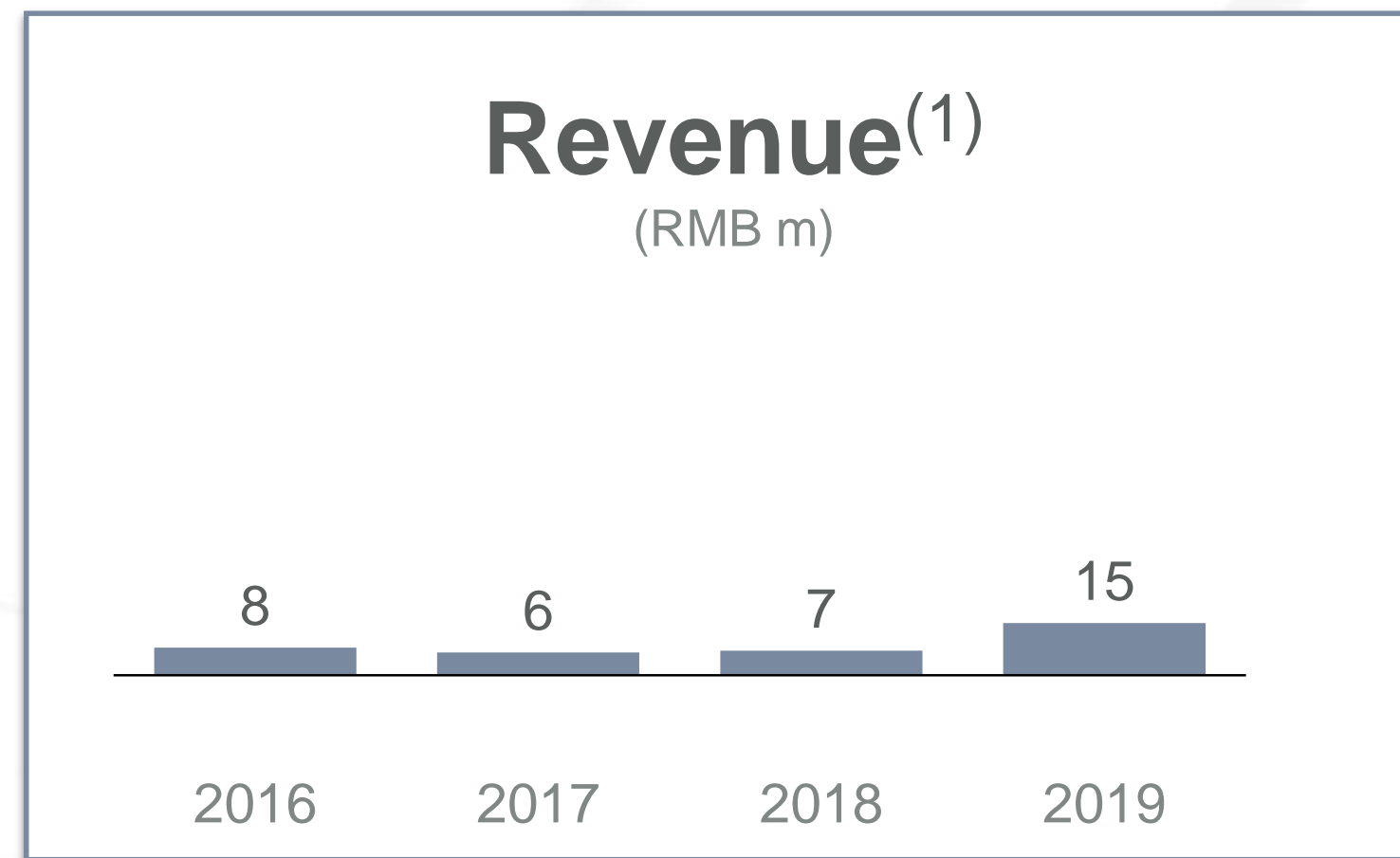
# Business Highlights for Fiscal Year 2019

- We have built a robust pipeline of eight clinical stage small molecule drug candidates. More than 30 Phase I or II clinical trials are ongoing in the United States, Australia and China.
- Core product candidate HQP1351 is under two pivotal Phase II clinical trials in China. We plan to submit NDA in China in 2020. HQP1351 has also entered into Phase Ib clinical trial in the United States.
- Key product candidate APG-2575 is under phase I trial in the United States and Australia. We have obtained approval from the U.S. FDA to start phase Ib/II clinical trials in CLL/SLL and WM patients. APG-2575 has also entered into Phase Ib clinical trial in AML in China.
- We have 80 issued patents and more than 200 patent applications globally, among which 67 patents had been issued overseas.





# Key Financial Highlights for Fiscal Year 2019



(1) The group derives its revenue from provision of research and development services, and compounds library and intellectual property license fee income;  
 (2) Adj. EBIT = Gross Profit + Other Income & expenses (excluding other gains & losses) – R&D Expense – Admin Expenses (excluding listing expenses)  
 (3) Cash & Equivalents include cash and bank balances, and other financial assets, which represent mainly investment in short-term financial products

# Robust Pipeline of Clinical Stage Drug Candidates

| Candidate     | Mechanism   | Lead Indications       | Preclinical                          | Ph I | Ph II | Countries        |                         |
|---------------|---|------------------------|--------------------------------------|------|-------|------------------|-------------------------|
| HQP1351       | BCR-ABL mutant  | Resistant CML          | [Progress bar: Preclinical to Ph II] |      |       | pivotal phase II | China                   |
|               | KIT   | GIST                   | [Progress bar: Preclinical to Ph I]  |      |       |                  | China                   |
| APG-2575      | Bcl-2 Selective   | CLL/SLL                | [Progress bar: Preclinical to Ph II] |      |       |                  | China, U.S. & Australia |
|               |   | WM                     | [Progress bar: Preclinical to Ph II] |      |       |                  | U.S. & Australia        |
|               |   | AML                    | [Progress bar: Preclinical to Ph II] |      |       |                  | China                   |
| APG-1252      | Bcl-2/Bcl-xL  | SCLC/NSCLC             | [Progress bar: Preclinical to Ph II] |      |       |                  | China, U.S. & Australia |
|               |   | NSCLC (Combo)          | [Progress bar: Preclinical to Ph II] |      |       |                  | China                   |
| APG-115       | MDM2-p53  | Solid tumors(IO combo) | [Progress bar: Preclinical to Ph II] |      |       |                  | China & U.S.            |
|               |   | AML                    | [Progress bar: Preclinical to Ph I]  |      |       |                  | China & U.S.            |
| APG-1387      | IAP Dimer   | Solid tumors(IO combo) | [Progress bar: Preclinical to Ph II] |      |       |                  | China & U.S.            |
|               |   | Hepatitis B            | [Progress bar: Preclinical to Ph II] |      |       |                  | China                   |
| AT-101        | Bcl-2/Bcl-xL/Mcl-1  | CLL                    | [Progress bar: Preclinical to Ph II] |      |       |                  | China & U.S.            |
| APG-2449      | FAK/ALK/ROS1  | NSCLC                  | [Progress bar: Preclinical to Ph I]  |      |       |                  | China                   |
| HQP8361       | c-Met selective   | Cancer (c-Met+)        | [Progress bar: Preclinical to Ph I]  |      |       |                  | China                   |
| Bcl-2 related | Strategic relationship with Unity to develop senolytic drugs. |                        |                                      |      |       |                  | U.S.                    |



# Global Clinical Development for Major Oncology Opportunities

Ascentage received 21 IND approvals globally

## United States



- APG-2575 (CLL/SLL, WM)
- APG-1252 (SCLC, NSCLC, Myelofibrosis - MF)
- HQP1351 (Resistant CML)
- APG-1387 (Solid tumors-IO combo)
- APG-115 (AML, Advanced solid tumors-IO combo)
- AT-101 (Multiple myeloma - MM)

## China



- HQP1351 (Resistant CML, GIST)
- APG-2575 (AML)
- APG-1252 (SCLC, NSCLC)
- APG-1387 (Solid tumors-IO combo, CHB)
- APG-115 (Solid tumors-IO combo, Sarcoma, AML)
- HQP8361 (Tumors with cMET+)
- AT-101 (CLL and GBM)
- APG-2449 (NSCLC)

## Australia



- APG-1252 (SCLC, NSCLC)
- APG-2575 (CLL/SLL, WM)
- APG-1387 (Advanced solid tumors)

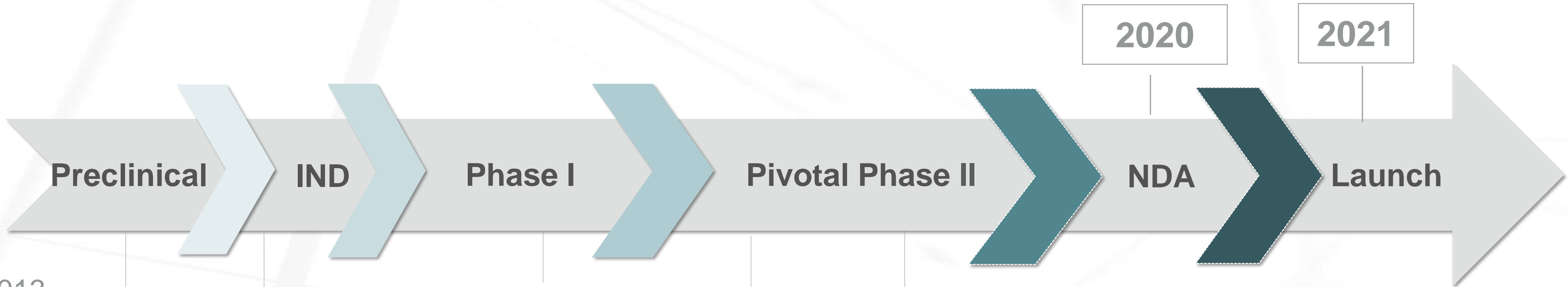
# IP Portfolio for Major Candidates in Clinical Pipeline

| Core Compound   | Patent Type   | Year Patent Expires |
|-----------------|---|---------------------|
| <b>APG-1252</b> | Product (Core compound structure); Process; Formulation; Combination; Use | 2034                |
| <b>APG-2575</b> | Product (Core compound structure); Combination                            | 2037                |
| <b>APG-115</b>  | Product (Core compound structure); Process; Combination; Use              | 2032-35             |
| <b>APG-1387</b> | Product (Core compound structure); New indication; Combination; Use       | 2033                |
| <b>HQP1351</b>  | Product (Core compound structure); Process; Combination; Use              | 2030-38             |



# HQP-1351

## 3rd-Gen BCR-ABL/KIT Multi-kinase Inhibitor



In June 2013, obtained exclusive rights related to HQP1351

In April 2015 submitted an IND TKI resistant CML to NMPA

In Feb 2016 , NMPA issued a "one-time umbrella approval" for rCML


In May 2019 , completed with data satisfying all endpoints for the primary and secondary objectives

In July 2019, FDA confirmed Phase Ib IND in US for TKI rCML

In July 2018 , held kick-off meeting with PI

In Jan 2019, awarded "National Major Innovative Drug Project" 

In Sep 2019, finished the enrollment of 2 pivotal Phase II Clinical trials

In Dec 2019, presented at ASH 2019 and nominated as "Best of ASH" 



# Well-tolerated with Minimal Drug Interruptions

## Ph I: HQP1351 well-tolerated

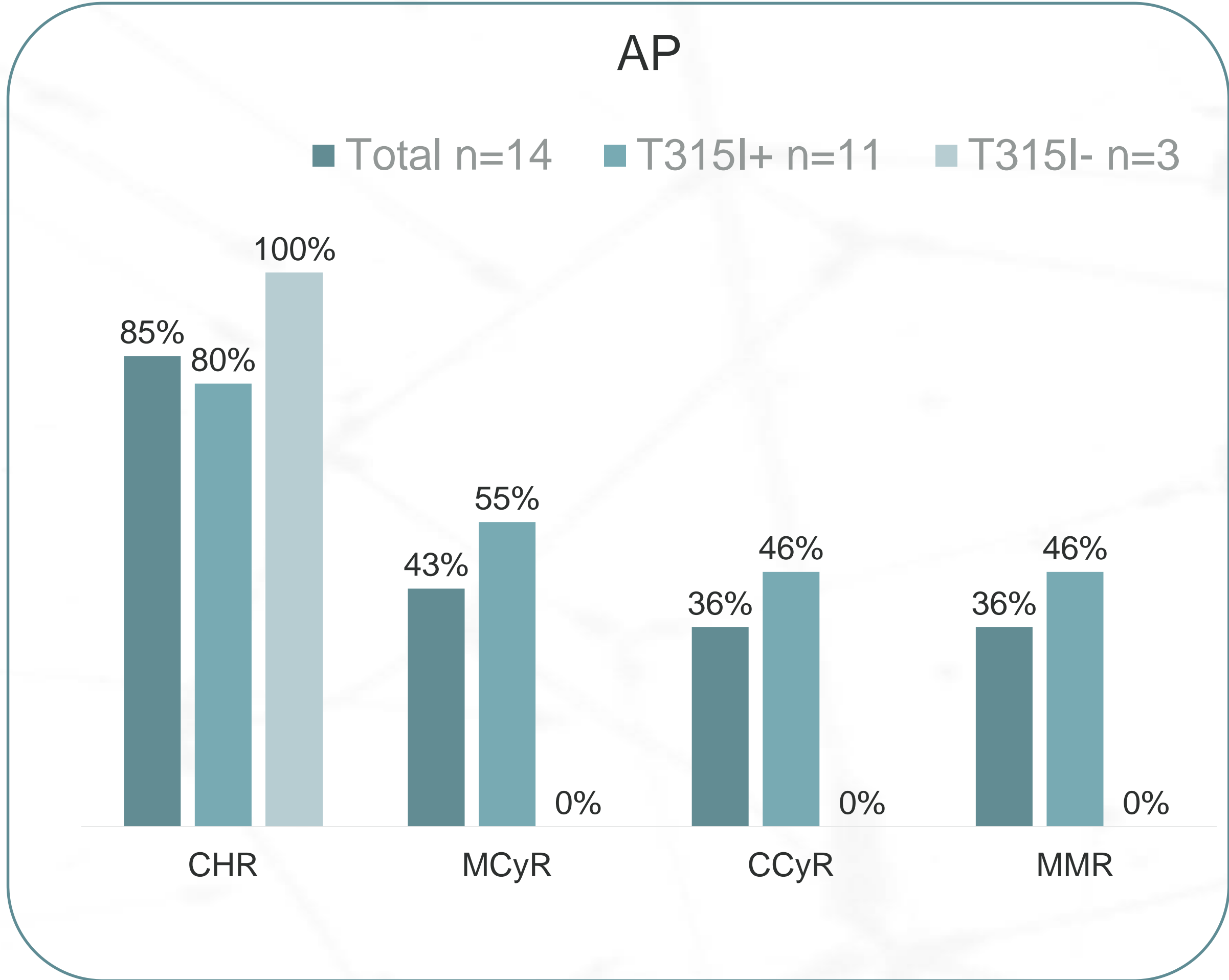
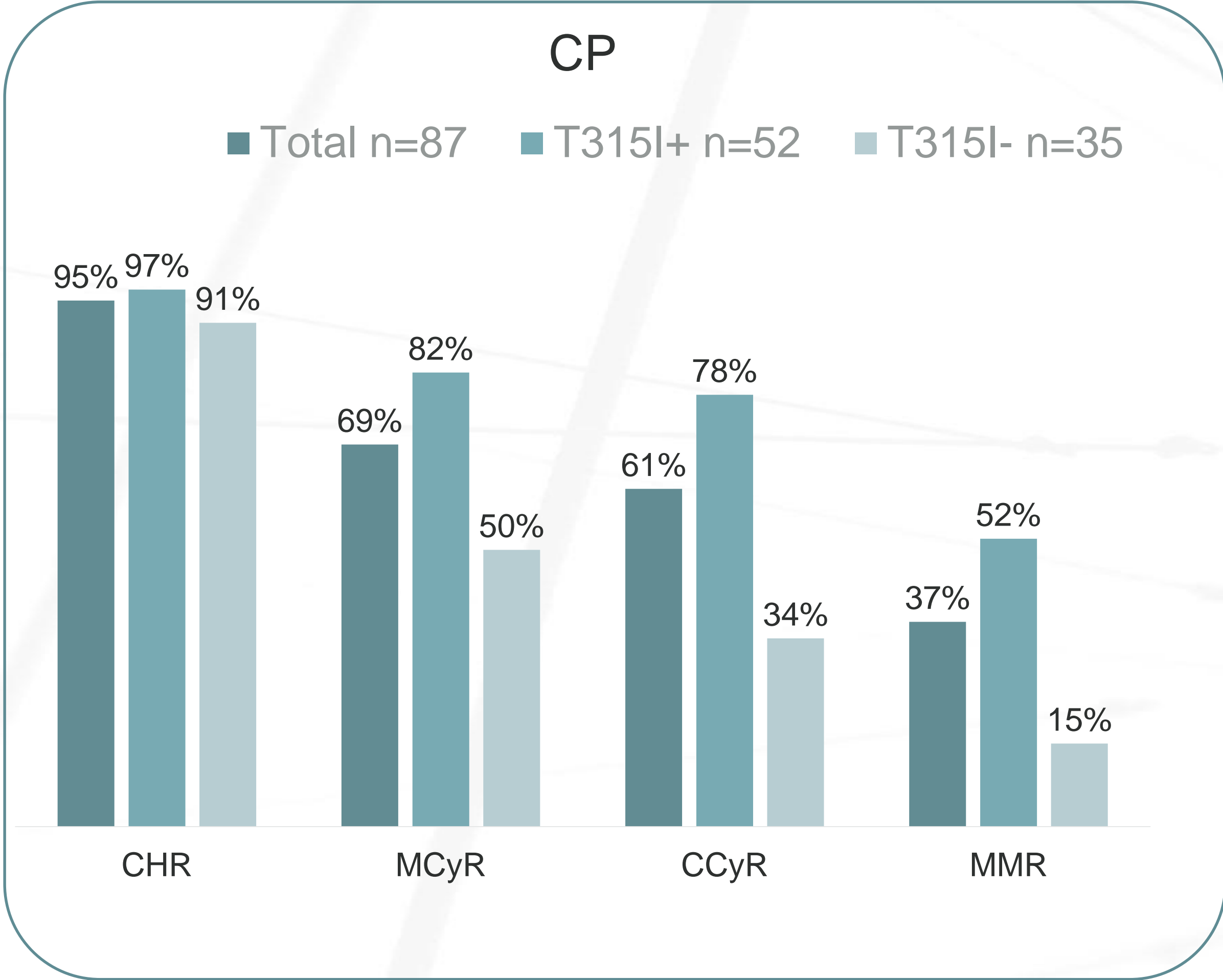
- 92 out of 101 patients have finished three cycles of treatment:
  - Longest duration of treatment is 31 months
  - The average observation period for the Ph I clinical trial is more than 1 year
  - 2 out of 101 patients has discontinued treatment due to AEs
- Most treatment-related AEs were mild or moderate**
- Grade 3 or 4 thrombocytopenia reported in HQP1351 treated patients
- No** cardiovascular, cerebrovascular, or peripheral vascular thrombosis, including fatal myocardial infarction or stroke was reported,
- The liver toxicity was rarely reported and was mild or moderate

### Summary of all Grade 3&4 AEs and SAEs in overall subjects

| AE (>10% of Patients) | Grade 3, 4 n(%) | SAE n (%) |
|-----------------------|-----------------|-----------|
| Thrombocytopenia      | 50 (49.5)       | 6 (5.9)   |
| Leukopenia            | 20 (19.8)       | 0 (0)     |
| Anemia                | 12 (11.9)       | 2 (2)     |
| Hypertriglyceridemia  | 8 (7.9)         | 0 (0)     |
| ALT elevation         | 2 (2)           | 0 (0)     |
| AST elevation         | 3 (3)           | 0 (0)     |
| Hyperbilirubinemia    | 1 (1)           | 0 (0)     |
| Proteinuria           | 5 (5)           | 0 (0)     |
| CPK elevation         | 2 (2)           | 0 (0)     |
| Pyrexia               | 7 (6.9)         | 1 (1)     |
| Rash                  | 2 (2)           | 0 (0)     |
| Skin Mass             | 1(1)            | 0 (0)     |



# Responses in Total Patients





# CML Patient Numbers

**51,000+**  
CML patients in US

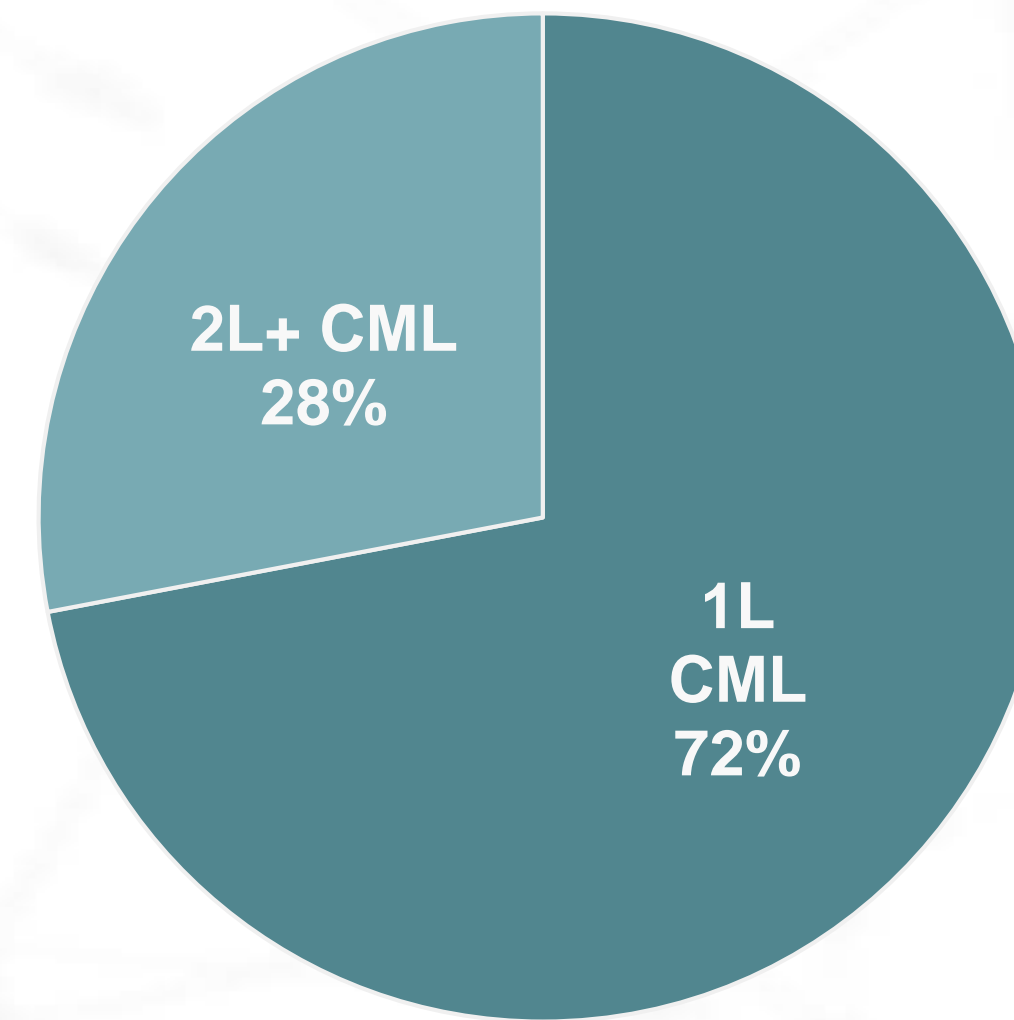


**75,000+**  
CML patients in China



Over 25% of patients with BCR-ABL-mutated CML have the T315I mutation<sup>2</sup>, which has been associated with resistance to treatment and poor outcomes<sup>3</sup>

## China's CML patient by lines of treatment





## Clinical Development

- **Phase I trail of APG-2575 for hematologic malignancies in US and Australia are ongoing**

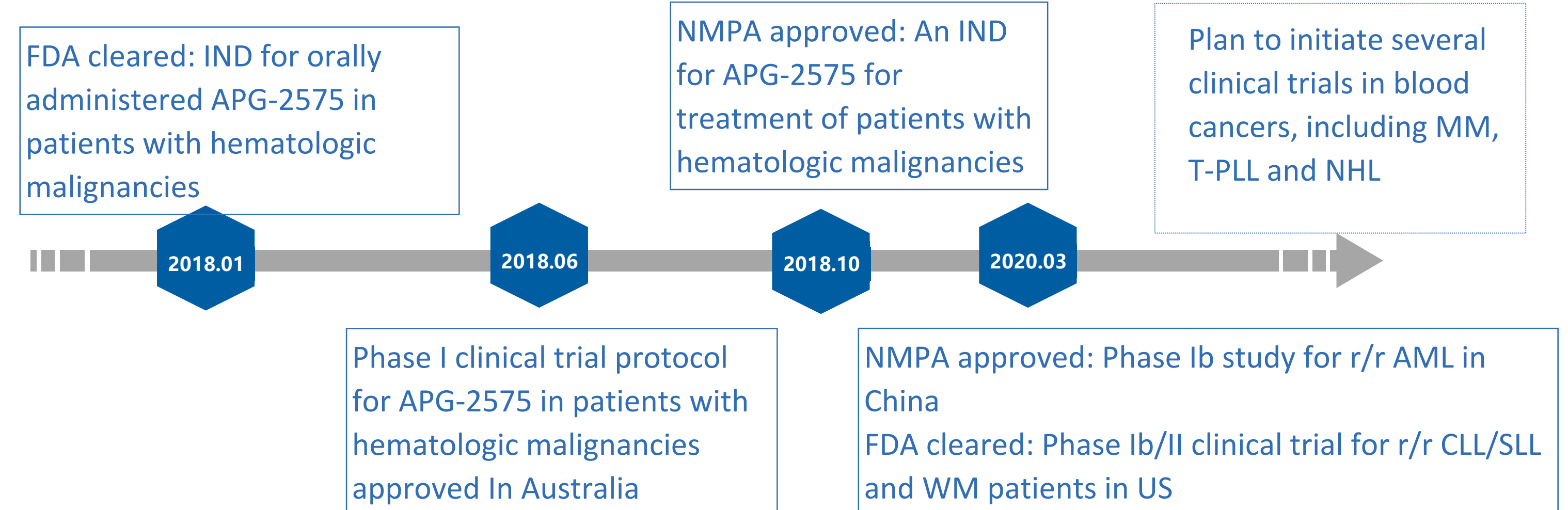
As of February,2020, total 19 patients enrolled in the two dose escalation trials  
Six dose levels completed, from 20mg to 600mg

- **Phase I trail in China, the third dose level is ongoing**

# APG-2575

A Bcl-2 Selective Inhibitor

## Milestone





# APG-2575

## Clinical Development

### Clinical Progress

#### Trial 1 - U.S. & Australia

- 15 patients with hematologic malignancies have been treated with APG-2575 at 6 dose levels
  - All 6 CLL patients completed the daily dose ramp-up without TLS.
  - 4 CLL patients have reached a criteria for hematological CR (ALC)
  - 2 CLL patients have reached PR (lymph node & ALC)
- Interim data shows APG-2575 is well-tolerated
- No DLTs, and No TLS and the MTD not reached

#### Trial 2 - China

- 4 patients have completed the first cycle of treatment
- No Serious Adverse Reaction

#### NMPA approved Phase Ib study for r/r AML in China

#### FDA cleared Phase Ib/II clinical trial for r/r CLL/SLL and WM patients in US

### Safety Profile

#### Drug Related Clinically Significant Events (n=8)

| Adverse Events                        | Any Gr    | Gr 3-4    |
|---------------------------------------|-----------|-----------|
| Any AE                                | 6 (75%)   | 2 (25%)   |
| Any DLT                               | 0%        | 0         |
| AE leading to hold or discontinuation | 1 (12.5%) | 1 (12.5%) |
| TLS or Laboratory TLS                 | 0         | 0         |
| Fatigue                               | 2 (25%)   |           |
| Lipase Increased                      | 2 (25%)   | 1 (12.5%) |
| Dermatitis allergic                   | 1 (12.5%) |           |
| Dyspnea                               | 1 (12.5%) |           |
| Pruritus                              | 1 (12.5%) |           |
| Sinusitis                             | 1 (12.5%) |           |
| Neutropenia <sup>□</sup>              | 1 (12.5%) | 1 (12.5%) |

<sup>□</sup> 008 experienced a Gr 3 neutropenia and led to dose interruption. ANC recovered to  $1.15 \times 10^9/L$  after holding on the IP for 8 days.



# APG-2575 and Venetoclax

## Differences Compared to Venetoclax:

- Preclinical data
- **No TLS**
- **Daily ramp-up** vs. weekly ramp up
- **Short  $T_{1/2}$  & AUC**--potentially lower risk of TLS with better safety profile

## When Selectively Targeting BCL-2



Dose Escalation (Daily Ramp)

PK Properties ( $T_{1/2}$  AUC)

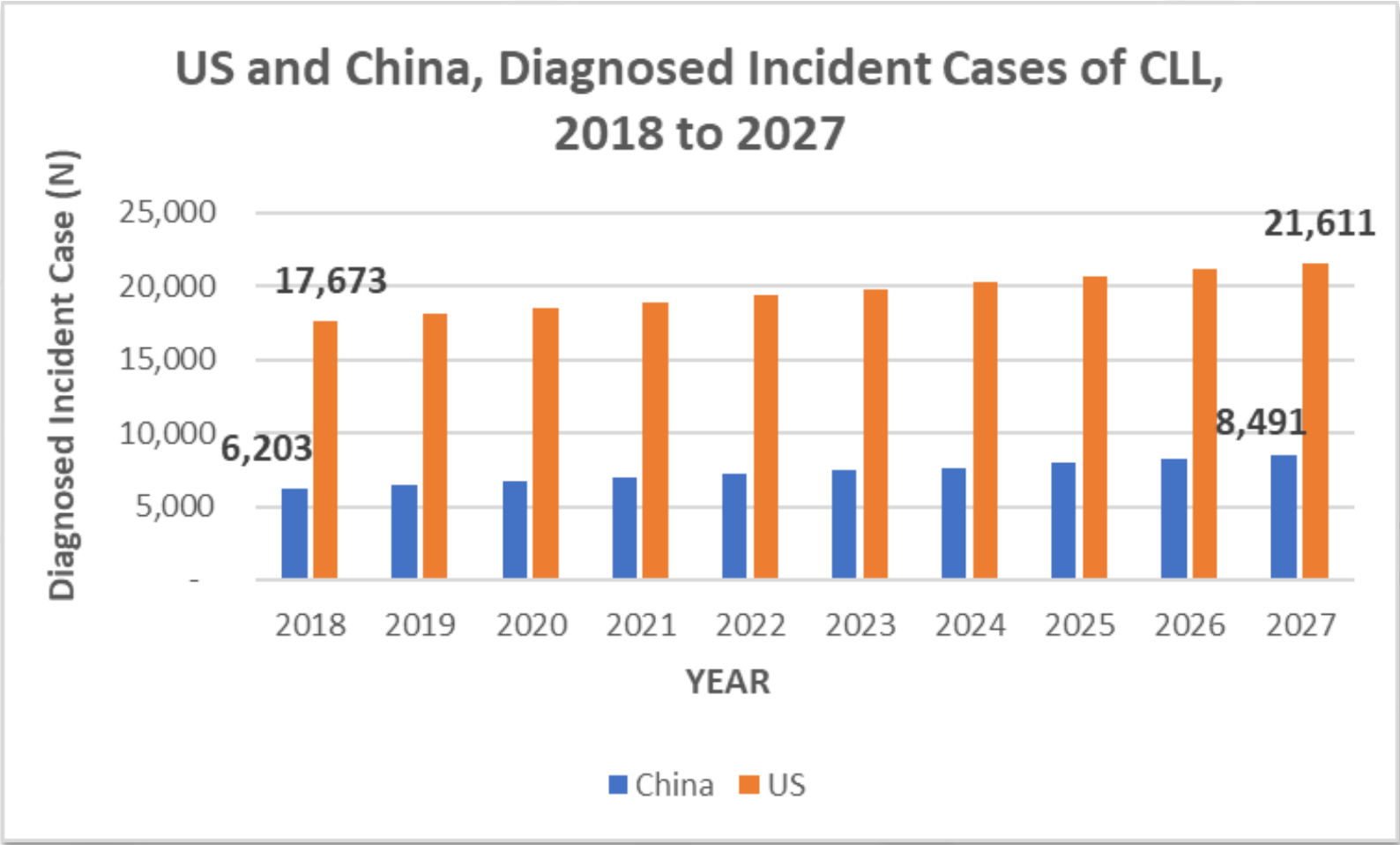
Safety: TLS, DDI



# Epidemiology Overview

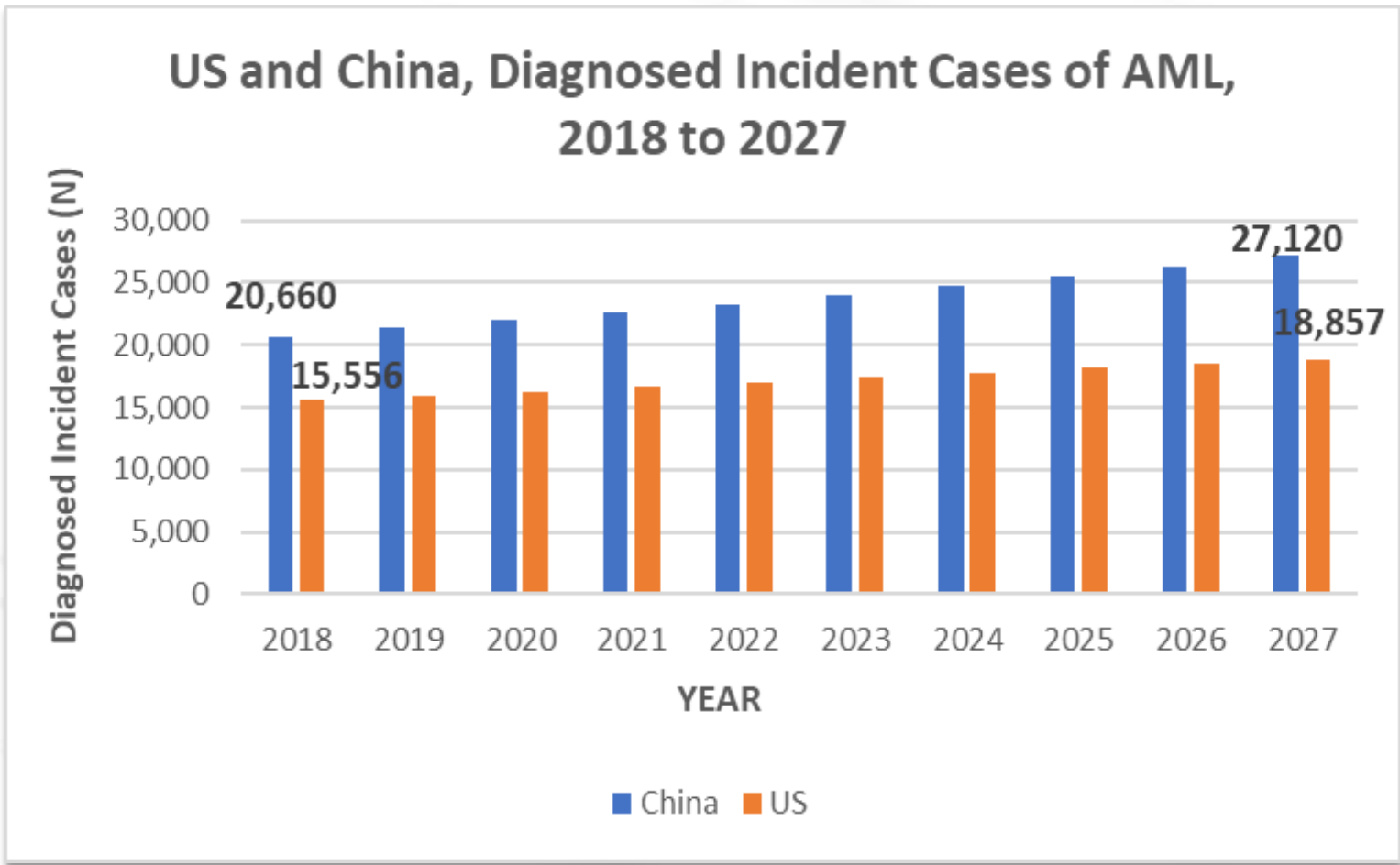
## CLL,AML,WM

### CLL



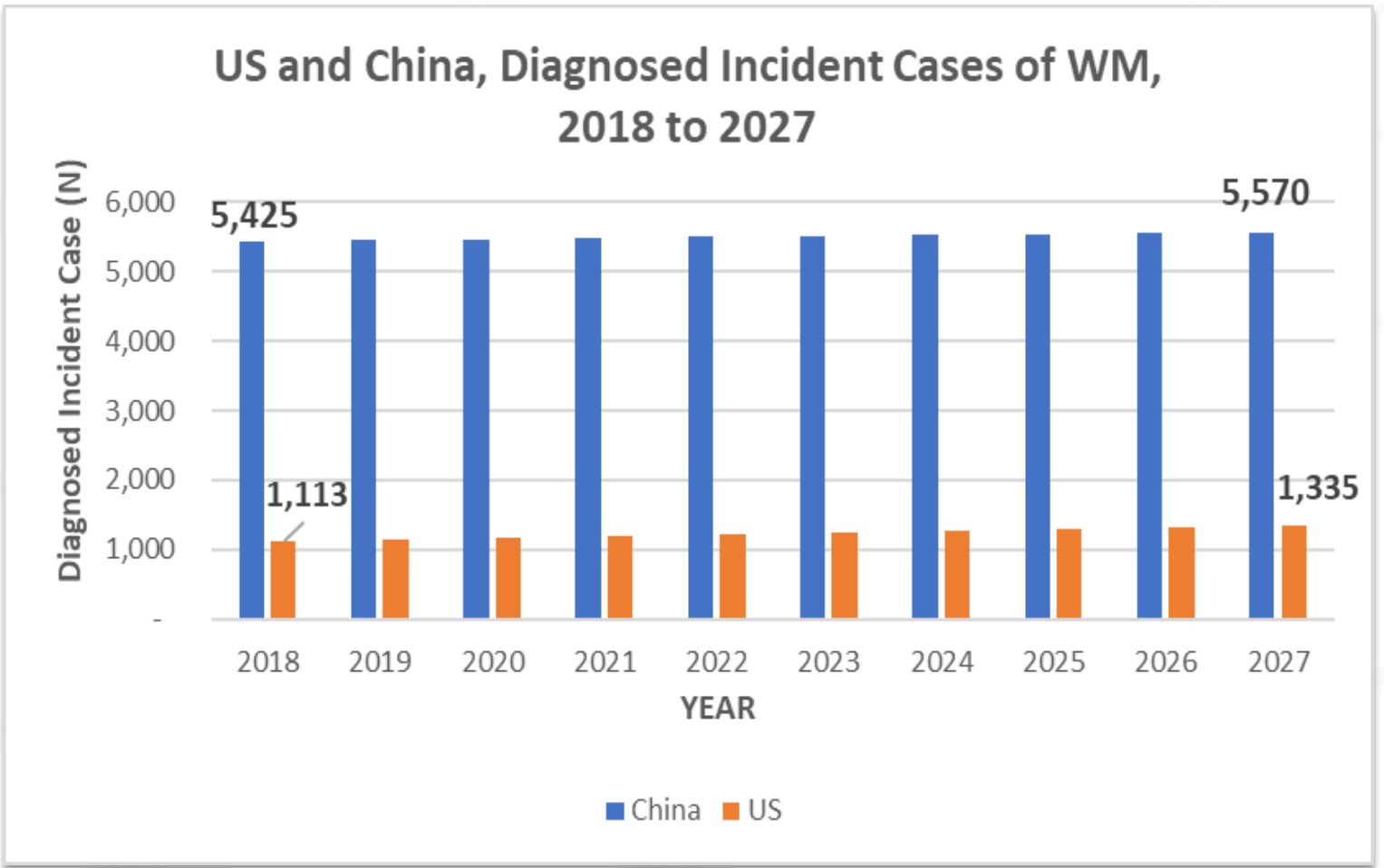
**2018-2027**  
**US CAGR 2.0%**  
**China CAGR 3.2%**

### AML



**2018-2027**  
**US CAGR 1.9%**  
**China CAGR 2.8%**

### WM



**2018-2027**  
**US CAGR 1.8%**  
**China CAGR 0.3%**



## Clinical Development

- **Two Phase I dose-escalation trials in patients with advanced cancers in the United States and Australia ongoing**
- **A Phase I dose-escalation/expansion trial as a monotherapy in patients with SCLC in China ongoing**

65 Patients are involved in the dose escalation trials

## Milestone

- New IND submitted to FDA in Dec 2019: APG-1252 in combination with Paclitaxel for patients with SCLC
- Pending Phase I results, planning a Phase II trial in relapsed/refractory NSCLC, or r/r NSCLC, in the United States and China.

# APG-1252

A Bcl-2/Bcl-xL Dual Inhibitor



# APG-1252

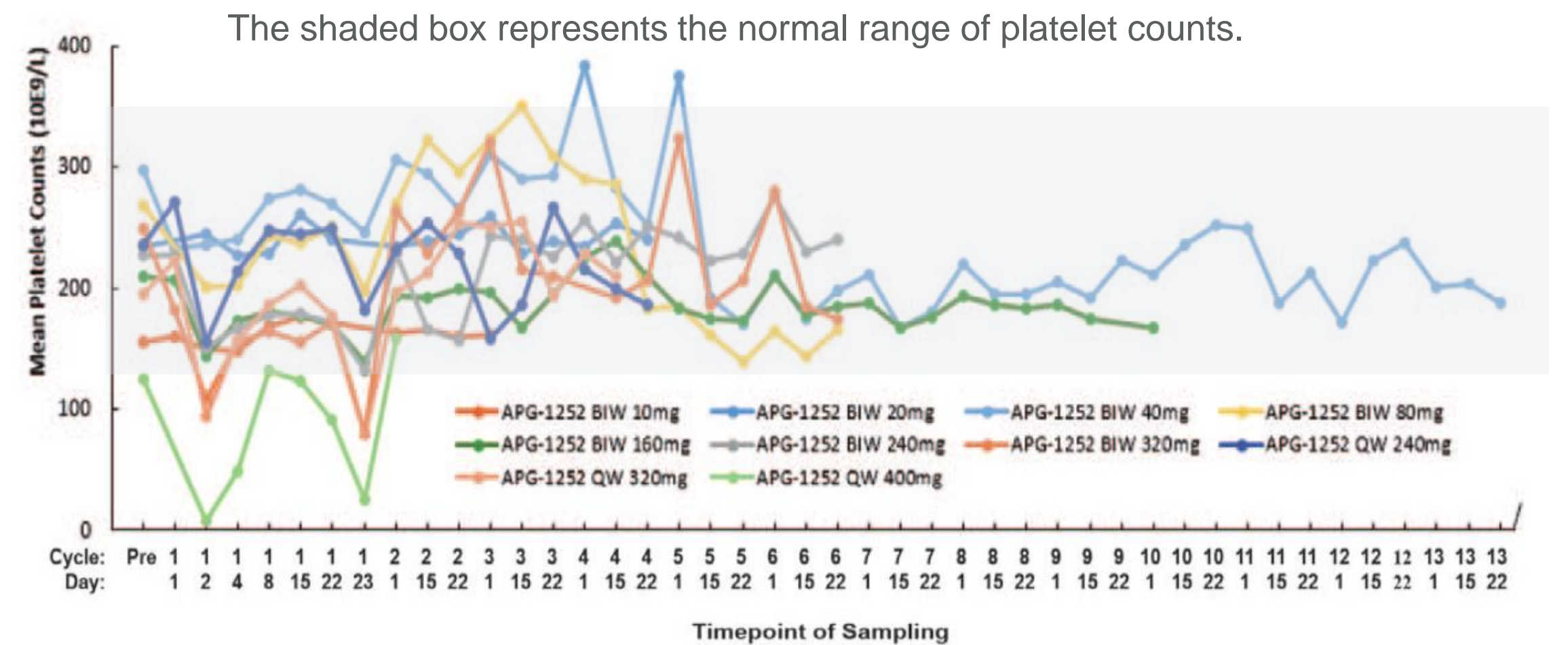
## Ph I Interim Data

### Anti-tumor Activity in SCLC

#### Dose Escalation Trial | N=65

- Dose escalation is ongoing
  - 8 cohorts
  - Dose range from 10-400 mg (twice weekly)
  - SCLC; n=29
    - 1 PR (in metastatic SCLC)
    - 4 SD after 2 cycles
  - Other Cancers; n=36
    - 2 PR (prostate with NET features)
    - 5 SD

#### No Significant Decrease in Platelet Count



Average platelet count value by patient treatment group over time



# Upcoming APG-1252 Clinical Development

- Initiate 3 PoC studies focus on various malignancies, provide evidence for go/no go decision for further development, explore potential registration pathway for Bcl-2/Bcl-xl inhibitor

2020

- Determine MTD and RP2D, optimize dosing schedule (weekly schedule)

- 1252 + chemo in 2nd line SCLC (FDA cleared, to be started)
- 1252 + osimertinib in 1st or 3rd line NSCLC: prevents/delays resistance to osimertinib in EGFR-T790M NSCLC (IND approved, China trial ongoing)
- 1252 + JAK2 inhibitor in myelofibrosis



# APG-1387

A Pan-IAP Inhibitor

## Clinical Development

- **The first IAP-targeting drug to enter clinical trials in China and Completed the Ph I clinical trial in solid tumors in Australia and China**
- Ph I demonstrates tolerability
- **A Phase I clinical trial in combination with pembrolizumab (“Keytruda”) in solid tumors ongoing**
- **A Phase Ib trial in naive Chronic Hepatitis B (CHB) patients completed the enrollment in China**

## Milestone

- In 2020, two Phase Ib/II clinical trials of APG-1387 combined with immuno-checkpoint inhibitor or chemotherapy in advance solid tumors have been approved
- Planning to initial a phase II clinical trial combo with NUC



# APG-1387 US Phase I Study on Cancers

Preliminary results showed efficacy in patients that relapsed after PD-1 treatment, or were unsuitable for PD-1 treatment, or failed PD-1 treatment. (cut-off date Dec.17th,2019)

| APG-1387         | Tumor Types       | Characteristics   | Best Response      | Assessment (Cycle #) |
|------------------|-------------------|---|--------------------|----------------------|
| <b>20mg N=4</b>  | Melanoma          | PD-1 treated, relapsed  | SD (-20%)          | C3D1                 |
| <b>30mg N=3</b>  | Breast cancer     | ER(+)<br>PR(-)<br>Her2 (-) with heavily previous treatments;<br>PD-1 untreated, MSS | <b>PR (-79.2%)</b> | C7D1                 |
|                  | Sarcoma of uterus | PD-1 untreated  | SD (+8.8%)         | C3D1                 |
| <b>45mg N=23</b> | CRC               | MSS, PD-L1 (-)  | SD (-18.7%)        | C9D1                 |
|                  | CRC               | Pembrolizumab failed, MSS   | SD (-11.8%)        | C5D1                 |
|                  | CRC               | PD-1 untreated MSS  | SD (-2.7%)         | C3D1                 |
|                  | Breast cancer     | HR+her2- , PD-1 untreated   | SD (+9.6%)         | C3D1                 |
|                  | NSCLC,            | PD-L1(-)  | <b>PR (-65%)</b>   | C5D1                 |
|                  | NSCLC             | PD-1 relapsed   | SD (-8.6%)         | C3D1                 |
|                  | NSCLC             | PD-1 failure  | SD (-3%)           | C3D1                 |
|                  | CRC               | MSS   | SD (+4.3%)         | C3D1                 |
|                  | Breast cancer     | HR+/Her2-   | SD (-5.4%)         | C3D1                 |
|                  | NSCLC             | PD-1 failure  | SD (+5.6%)         | C3D1                 |

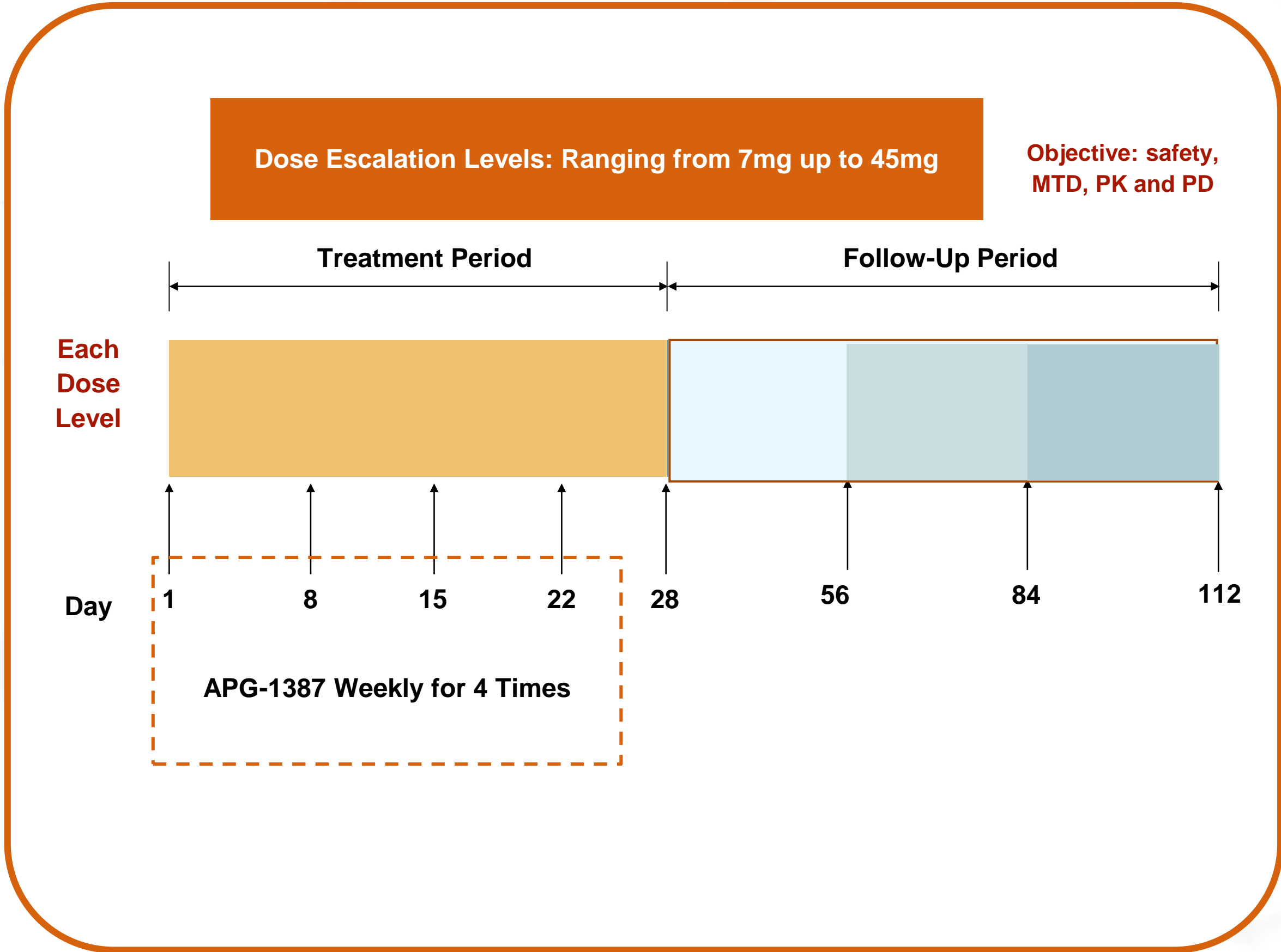


# APG-1387

## Hepatitis B Clinical Development

### Study Design of APG-1387 Monotherapy in CHB

### Favorable Safety and Efficacy



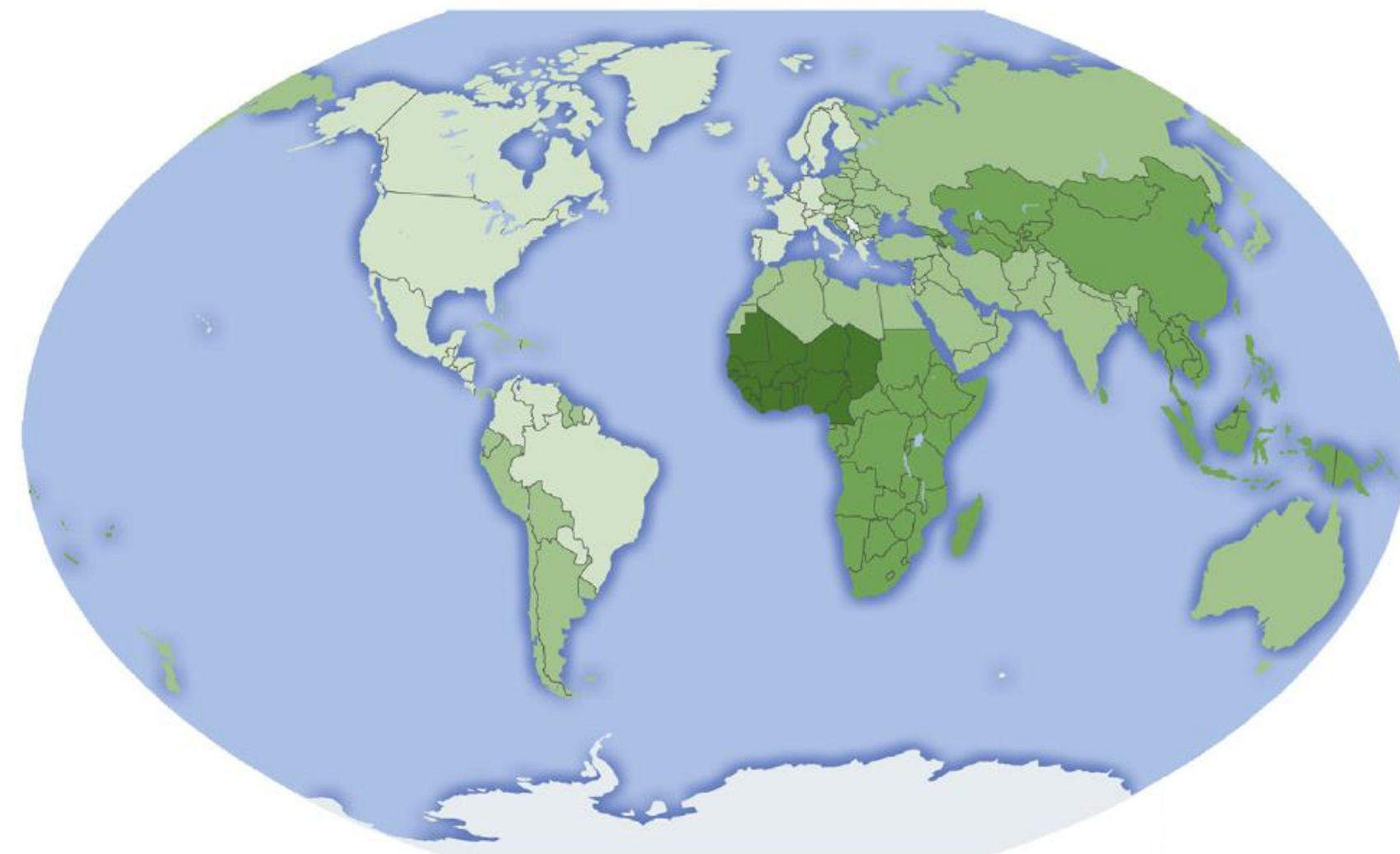
- As of December 31, 2019, a **total of 103** patients were involved in studies.
- The MTD has not yet been determined. No DLT was observed. All AEs were mild to moderate in severity (Gr 1 or 2)
- After just 4 doses & compared to baseline
  - HBV DNA levels declined in 23 out of 26 patients
  - HBsAg levels declined in 17 out of 26 patients
  - Some patients' HBV DNA and HBsAg levels continued to decline during the follow-up without further treatments

Source : Company data  
 Note: Study design for illustrative purpose only: actual clinical trial design may deviate from this illustrative chart

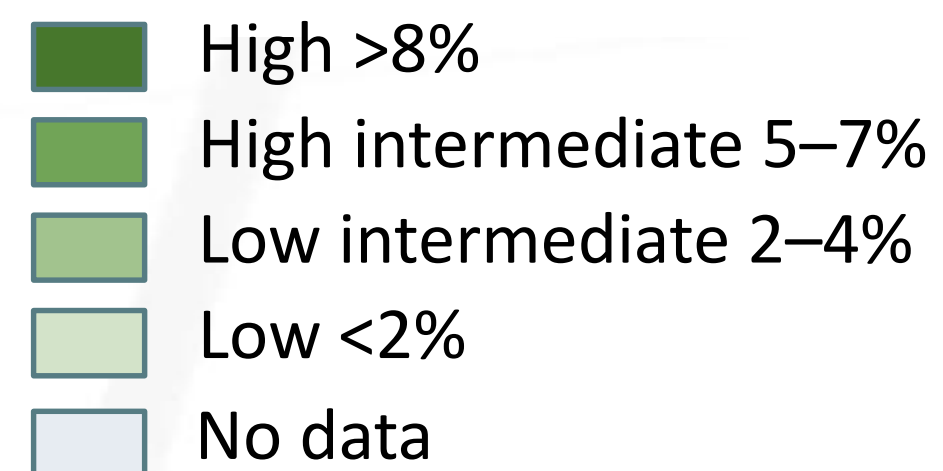


# HBV Remains a Major Global Health Problem

## Global trends in HBV infection<sup>1</sup>

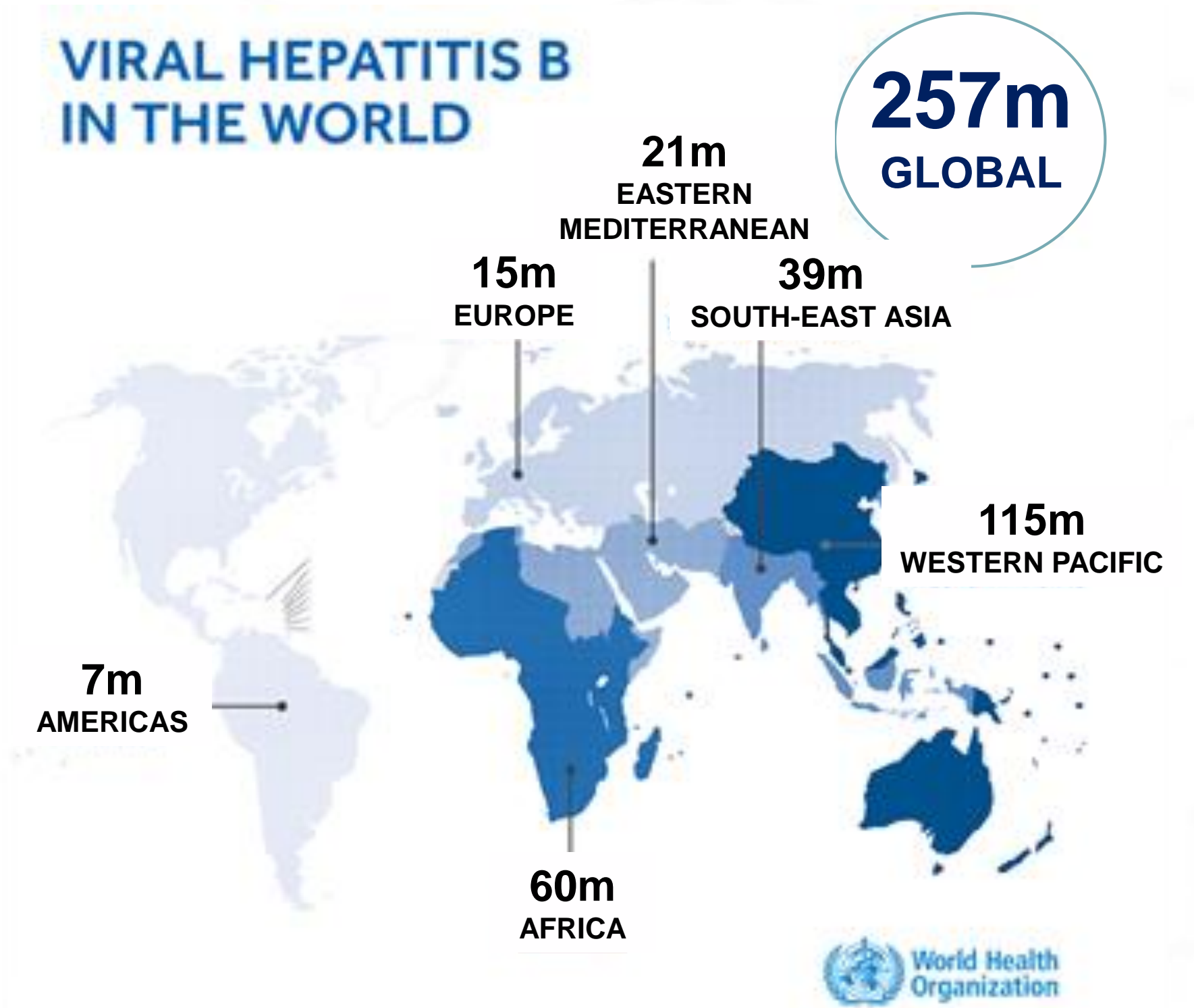


### Prevalence of hepatitis B



## Globally, 257 million people infected<sup>2</sup>

### VIRAL HEPATITIS B IN THE WORLD



1. Chang MS, Nguyen MH. Best Pract Res Clin Gastroenterol 2017;31:239–247;

2. WHO. Global hepatitis report 2017. Available at: <http://apps.who.int/iris/bitstream/10665/255016/1/9789241565455-eng.pdf?ua=1> (accessed March 2018); 3. Zhang WL, et al. Chin J Epidemiol 2017; 38(9): 1278



## Clinical Development

- **Two Phase I trials are ongoing in the U.S. and China, respectively in advanced solid tumors or lymphoma**
- Completed enrollment of the Ph I clinical trial (29 patients were treated) with 6 dose-escalation cohorts in the U.S.
- **A Ph Ib/II trial in combination with pembrolizumab in patients with advanced solid tumors is ongoing**
- 1 patient confirmed CR, 2 PRs were observed, 6 patients had SD as the best response; the total DCR is 64% with an ORR of 21%

## Milestone

- Made an oral presentation on the preliminary results at the International Congress on Targeted Anticancer Therapies by European Society for Medical Oncology in February 2019
- Phase Ib/II clinical trial for APG-115 in combination with chemotherapeutic or other targeted agents for the treatment of patients with hematologic malignancies was approved by the NMPA in China in July 2019
- Submitted an Orphan Drug Designation Application to the Office of Orphan Products Development of the FDA in February 2019
- We plan to submit additional INDs for combination trials in China and U.S.

# APG-115

## A MDM2-p53 Inhibitor



# APG-115

## Clinical Development Plan

### Study Design Dose Escalation of APG-115<sup>(1)</sup>

#### Objectives:

- Safety
- MTD/RP2D
- PK
- PD

#### Parts

- Dose escalation
- Cohort expansion



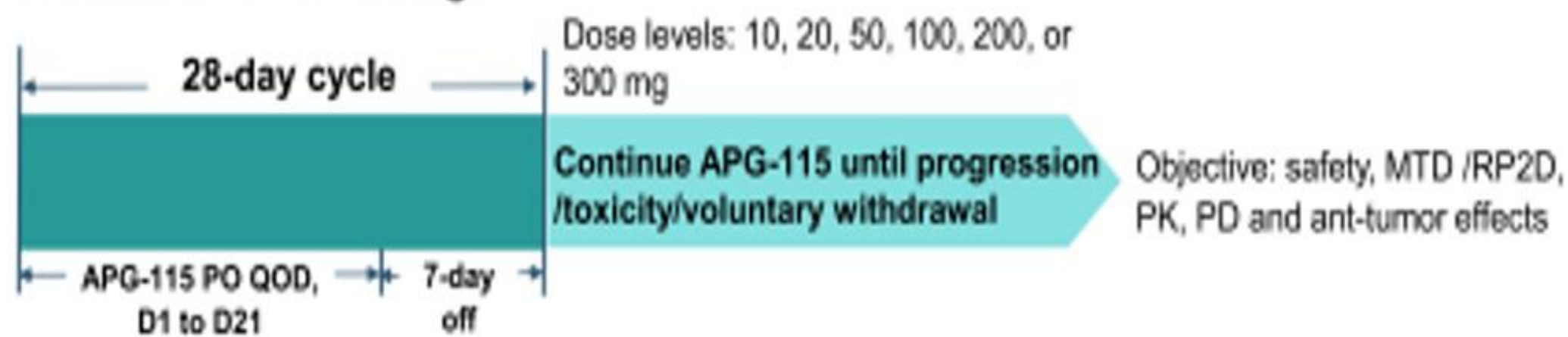
#### Part 1 - Dose Escalation

Levels from 10mg - 500mg over 28d

#### Part 2 - Cohort Expansion

Based on RP2D established in Part 1

**Phase I dose escalation study - accelerated dose escalation, then standard "3+3" design**



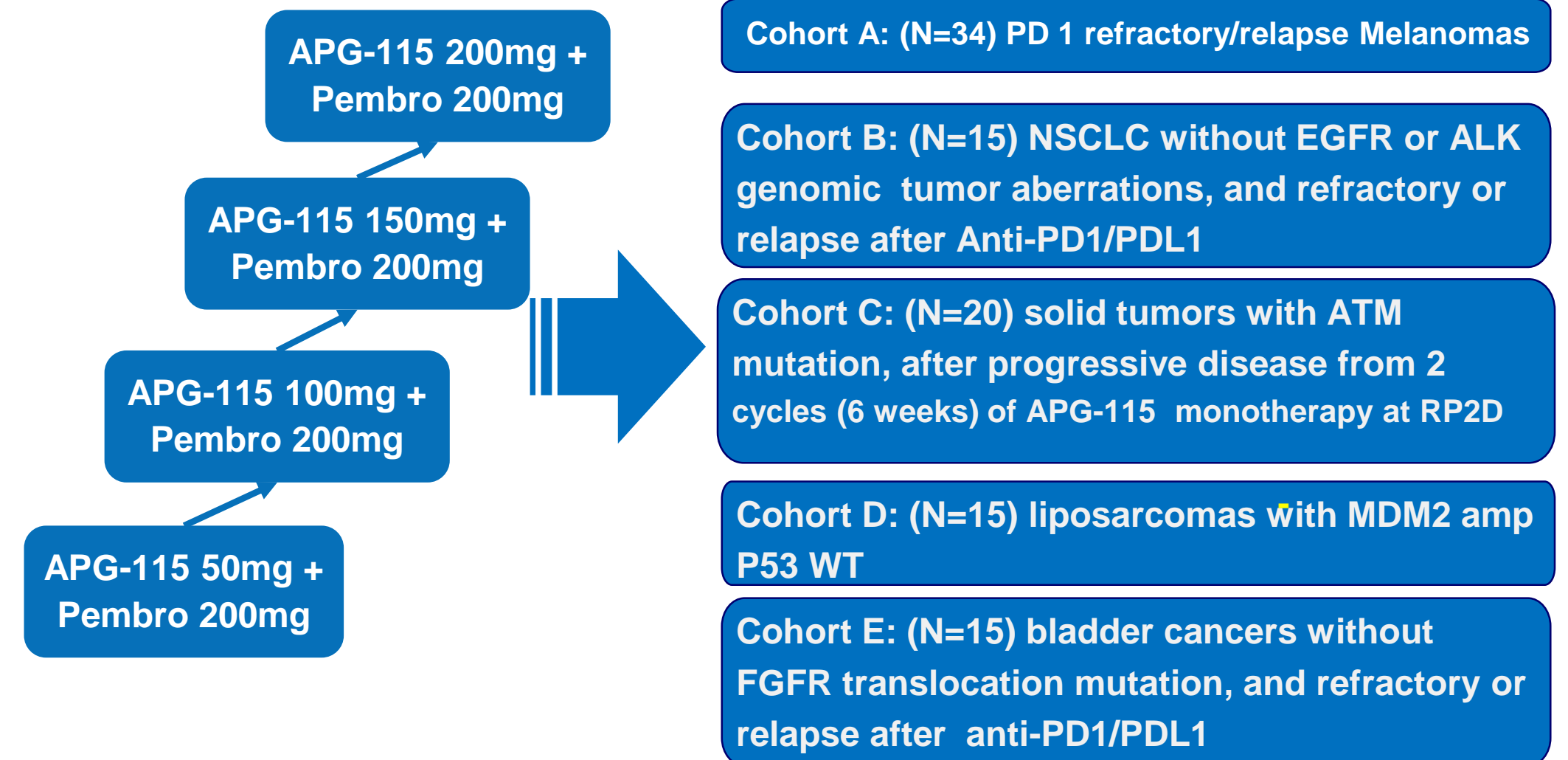
### Combination Trial with Keytruda (pembrolizumab)<sup>(2)</sup>

#### Parts

1. 3+3 dose escalation to identify MTD / RP2D
2. POC study with PD-1 in relapse/refractory melanoma, NSCLC, liposarcoma, bladder and other cancers

**APG-115 at 150 mg, QOD +Pembro 200 mg**

- POC study with 5 cohorts:



Source : Company data

Note: Study design for illustrative purpose only; actual clinical trial design may deviate from this illustrative chart

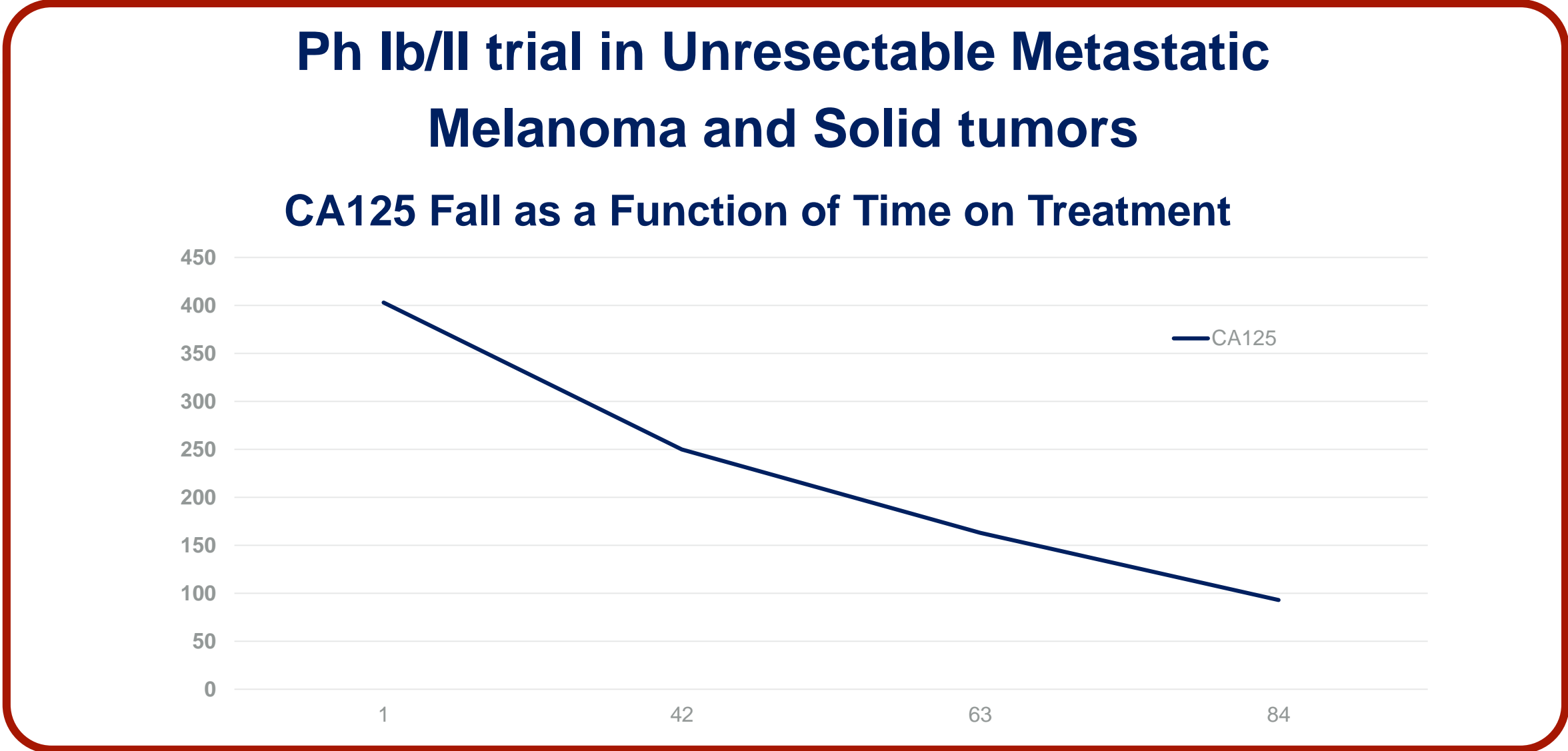
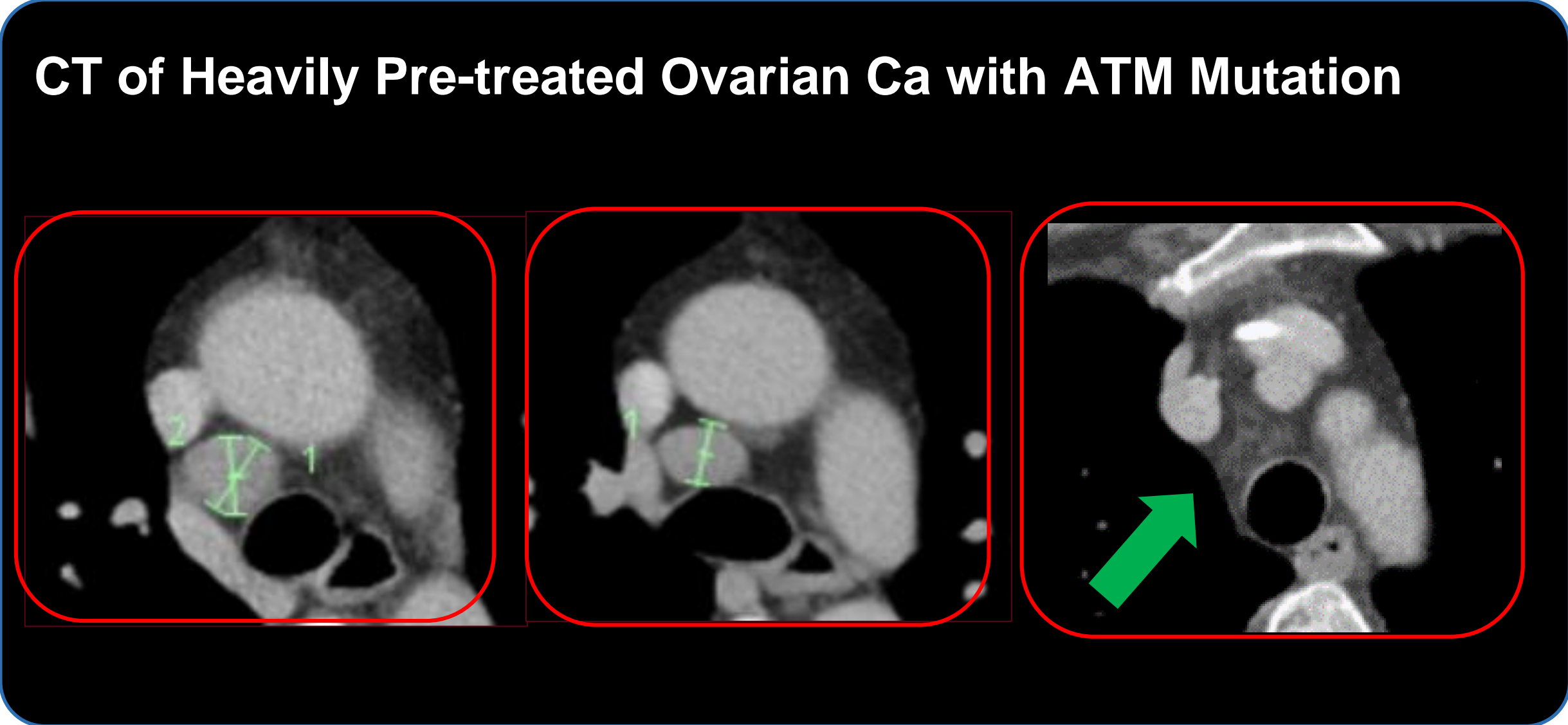
(1) Ph I Study design

(2) Ph Ib/II Study design



# APG-115 Shows Promise Efficacy Combined with pembrolizumab

APG-115 and Keytruda achieves a CR in heavily pre-treated, ATM-mutated Ovarian Cancer



### Treatment History

| Initial Tx  | Tx  | Clinical Trial                    |
|---|---|-----------------------------------|
| Neoadjuvant<br>• Paclitaxel<br>• Carboplatin<br>• TAH BSO | Adjuvant<br>• Carboplatin<br>• Docetaxel<br>Relapse < 6mo.<br>• Doxil<br>• Topotecan<br>• Bevacizumab<br>• PD XMT1536 | APG-115 (150 mg)<br>&<br>(200 mg) |

Trial to date (N=19) • 3 dosing cohorts: 50 mg | 100 mg | 150 mg

| Efficacy (N=14)                       | Safety  |
|---------------------------------------|---|
| 1CR   2PR   6SD<br>~21% ORR & 63% DCR | The combination is well-tolerated<br>No DLTs, No Additive AEs |

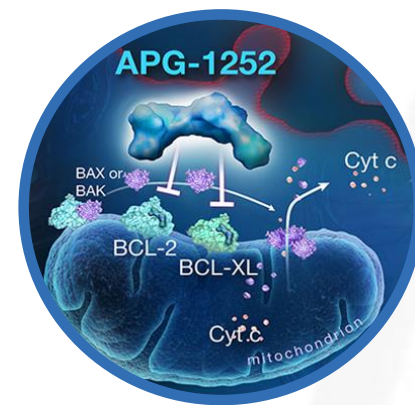
Source: Company data





# Strategic Alliances

Smart Collaborations Supported By The World's Leading Oncology Teaching Hospitals



BCL2



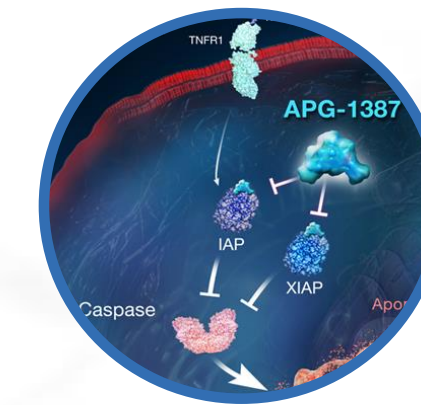
Henlius

Unity :

- Worldwide ex-China exclusive licensing in non-oncology diseases
- Joint venture option in China

Henlius :

- Clinical trials of the combination therapy between APG-2575, and Rituximab Injection for the treatment of CLL in the PRC



IAP



- Exclusive collaboration with TopAlliance
- Toripalimab (Tuoyi®) , the first anti-PD-1 mAb developed by a Chinese company and marketed in China
- Explore the synergies of APG-1387, and toripalimab, in clinical trials in solid and hematological tumors in China



Dana-Farber  
Cancer Institute

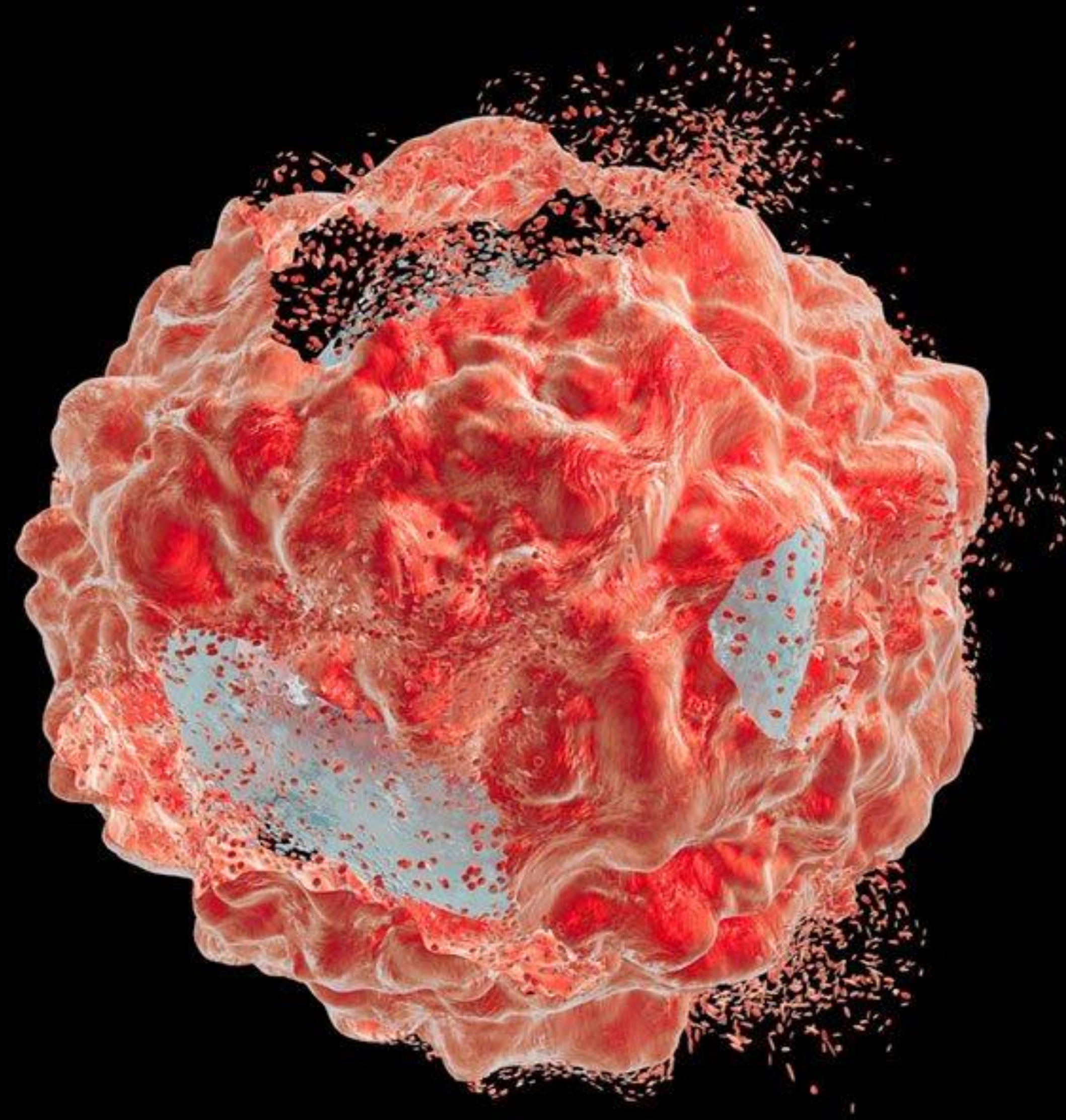


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# Ascentage Pharma Group

*Advancing Therapies That  
Restore Apoptosis*