

# Ascentage Pharma Group

Advancing Therapies That  
Restore Apoptosis

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# Ascentage: Innovative Science

Proprietary PPI Platform Delivering Potentially First and/or Best-in-class Drugs

## BREAKTHROUGH SCIENCE



**90+** ISSUED PATENTS  
**400+** PENDING APPLICATIONS  
**100+** PUBLICATIONS

## STRONG PIPELINE



**12** NOVEL COMPOUNDS  
**33** INDS  
**40+** CLINICAL TRIALS  
**10+** INDICATIONS

## DEDICATED TEAM



**1** VISION: BUILDING A GLOBAL BIOTECH COMPANY  
**20+** YEARS' COMMITMENT OF EXECUTIVE TEAM  
**400+** EMPLOYEES

## GLOBAL DEVELOPMENT

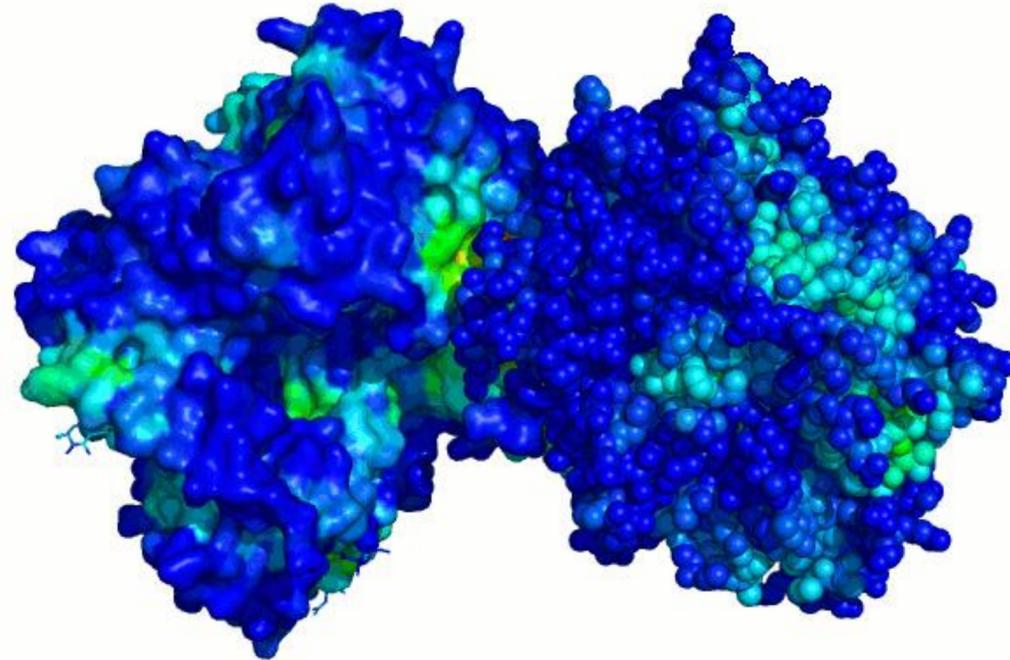


INTEGRATED ORGANIZATION IN **CHINA, UNITED STATES** AND **AUSTRALIA**

# Global Leader Developing Therapeutics That Inhibit Protein-protein Interactions to Restore Apoptosis

## Protein-protein Interactions

Protein-protein interactions (PPIs) play a crucial role in cellular processes, and are implicated in many diseases, from cancer to viral infections



## Focused on Apoptosis

Apoptosis plays a crucial role in developing and maintaining the health of the body by eliminating old and unhealthy cells.

## Difficult to Drug

PPIs have broad, shallow, relatively featureless binding sites, hence historically **“difficult to drug”**. There is only one PPI-targeting drug approved in oncology, Venetoclax.

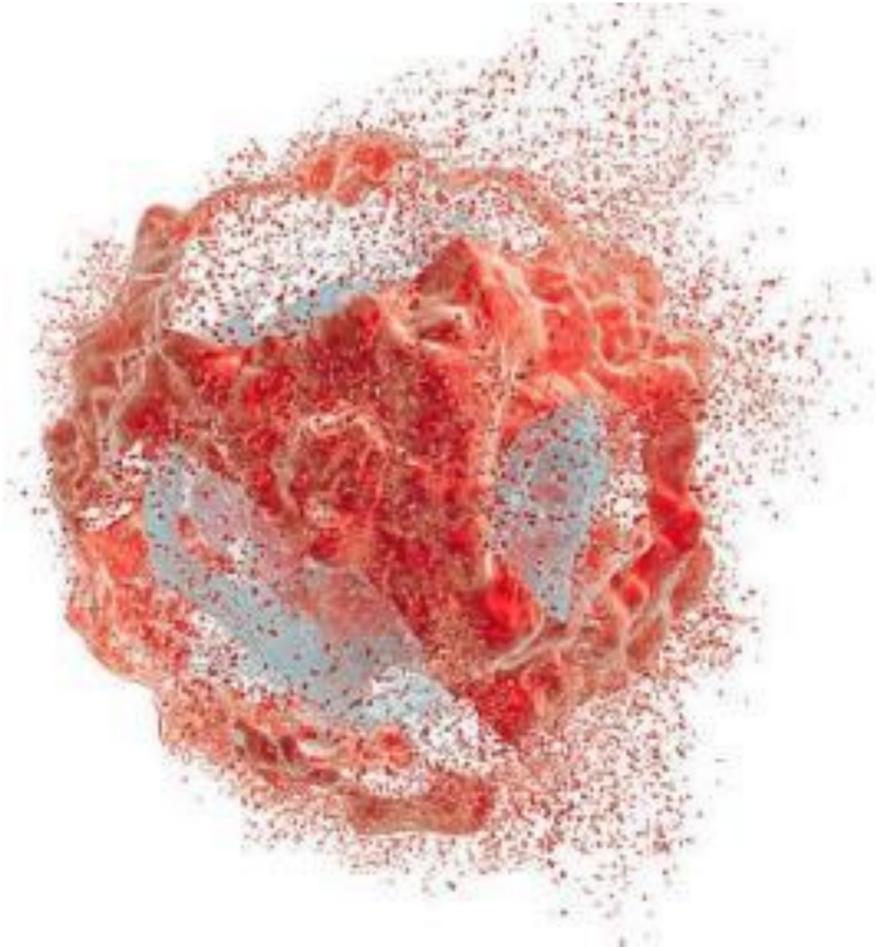
## Small Molecules

PPI targets can't be penetrated by large molecules, leaving small molecules the only viable choice for drug development PPI

## Targeting Bcl-2, MDM2-p53, IAP

**Four** potentially **first- or best-in-class** candidates targeting three distinct classes of PPIs that are critical in inducing apoptosis, namely, Bcl-2, MDM2-p53 and IAP proteins.

# 2020 Key Achievements



- **1 NDA with “Priority Review”** for HQP1351 (Olverembatinib)
- **Clinical Proof of Concept (POC)** of APG-2575 established in r/r CLL
- **9 global studies** of APG-2575 in CLL , AML , MM etc.; entered Europe for the first time
- **9 ODD and 1 FTD** (HQP1351 in TKI resistant CML)
- **2 global clinical collaborations** with AstraZeneca and Merck

# Rich Pipeline With Significant Opportunities

Product	Target	Indications	Phase I	Phase II	Pivotal	NDA	Regions
HQP1351	BCR-ABL /KIT	CML	CDE-NDA submission mid-2020				 
		Ph+ ALL					
APG-2575	Bcl-2	CLL					
		WM					
		MM					
		T-PLL					
		AML					
	Solid Tumors						
APG-115	MDM2-p53	Solid Tumor + IO					
		AML, MDS					
APG-1387	IAP/XIAP	Solid Tumor + IO					
		PDAC + Chemo					
		HBV					
APG-1252	Bcl-2/xL	SCLC + SOC					
		NSCLC + TKI					
		MF					
		NET					
APG-2449	FAK/ALK/ROS1	Solid Tumor					
Bcl-2 product	Bcl-2 family	DME (developed by Unity)					

 POC  POC in progress

# More ODDs Than Any Other Chinese Biotech Companies

4

Breakthrough



Zanubrutinib  
1 BTD



JS001  
1 BTD



Sugemalimab  
1 BTD



RC48-ADC  
1 BTD

36

Orphan Drug



APG 115, APG 1252,  
APG 2575, HQP1351  
**9 ODDs**



Zanubrutinib,  
Tislelizumab  
4 ODDs



JS001  
3 ODDs



YS-ON-001  
3 ODDs



15

Fast Track



HQP1351  
1 FTD



Abexinostat  
2 FTDs



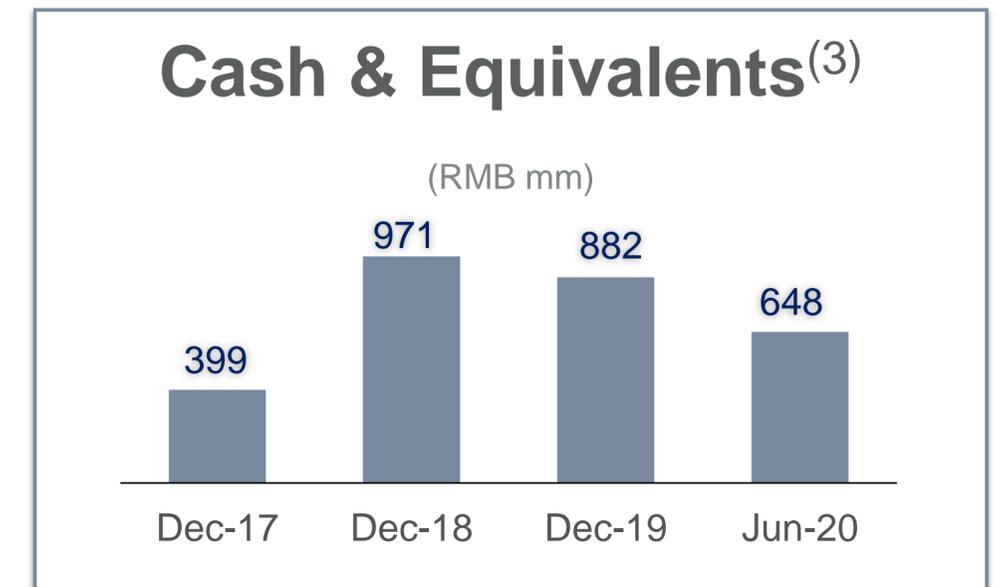
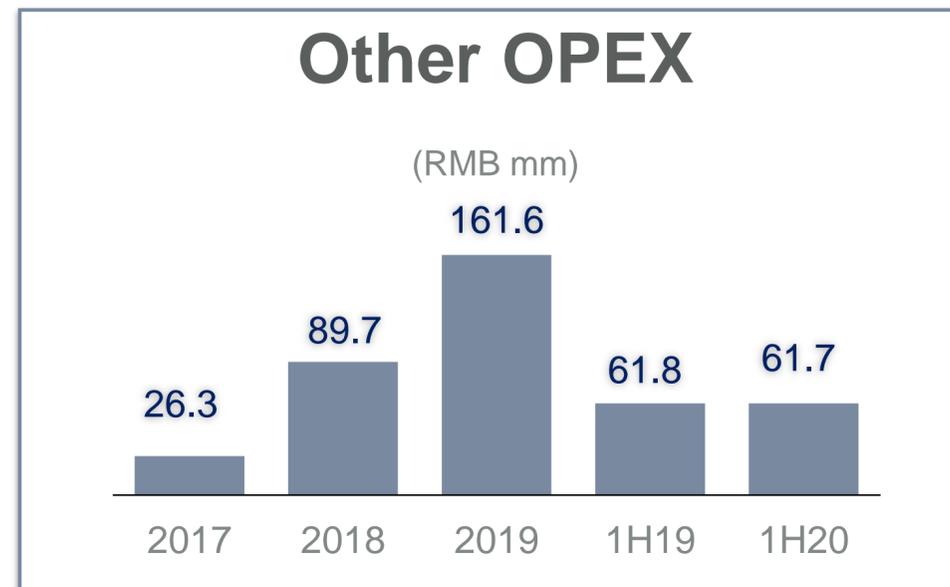
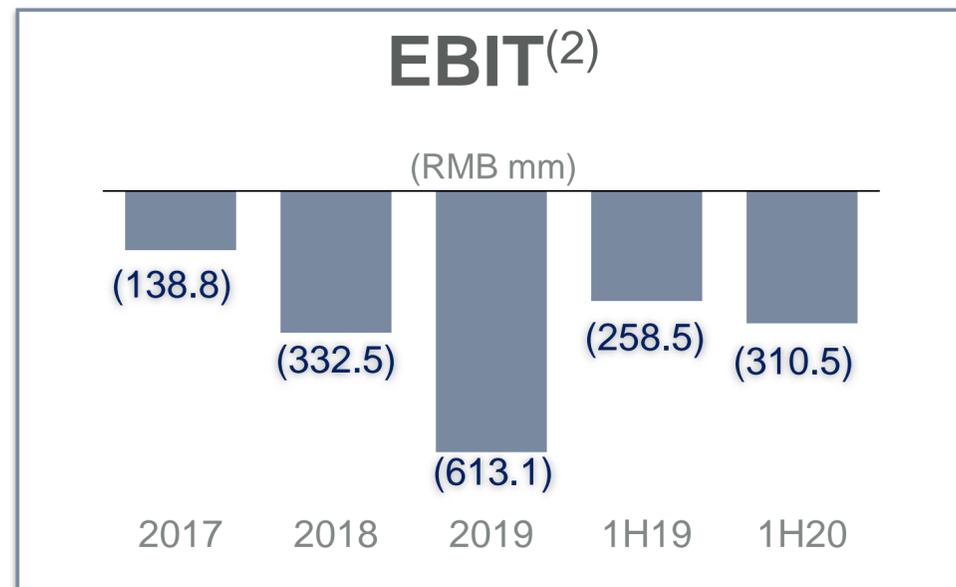
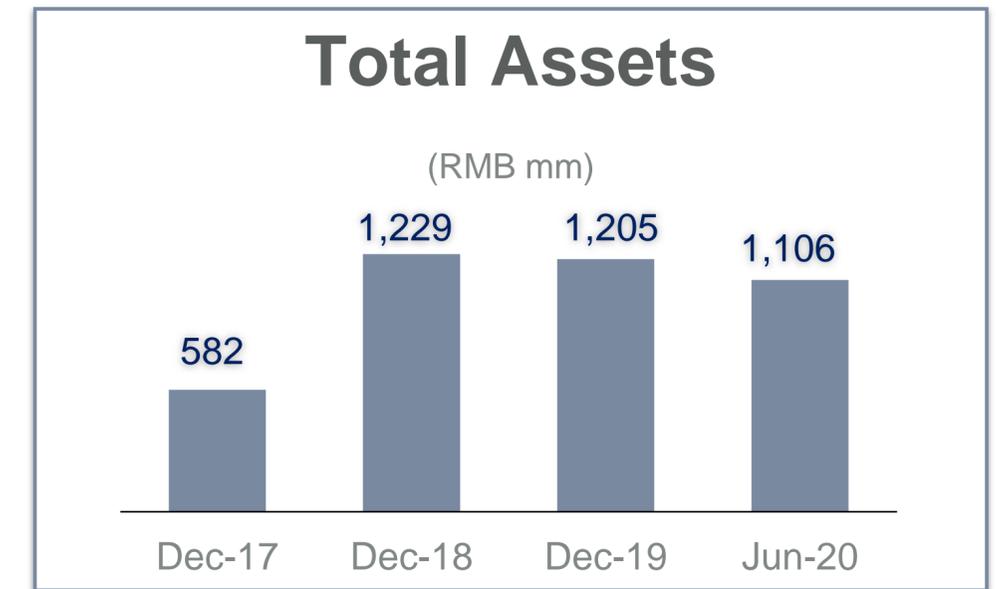
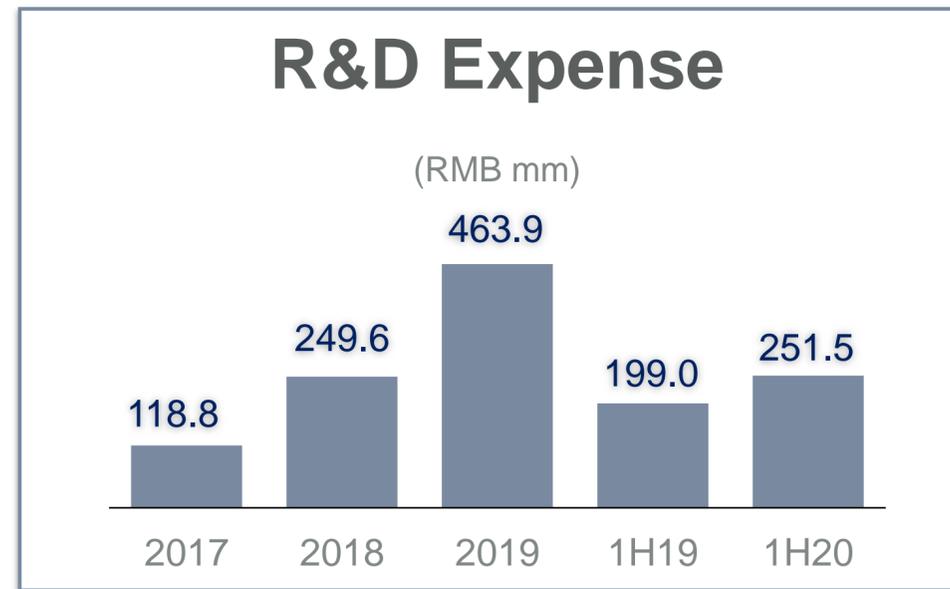
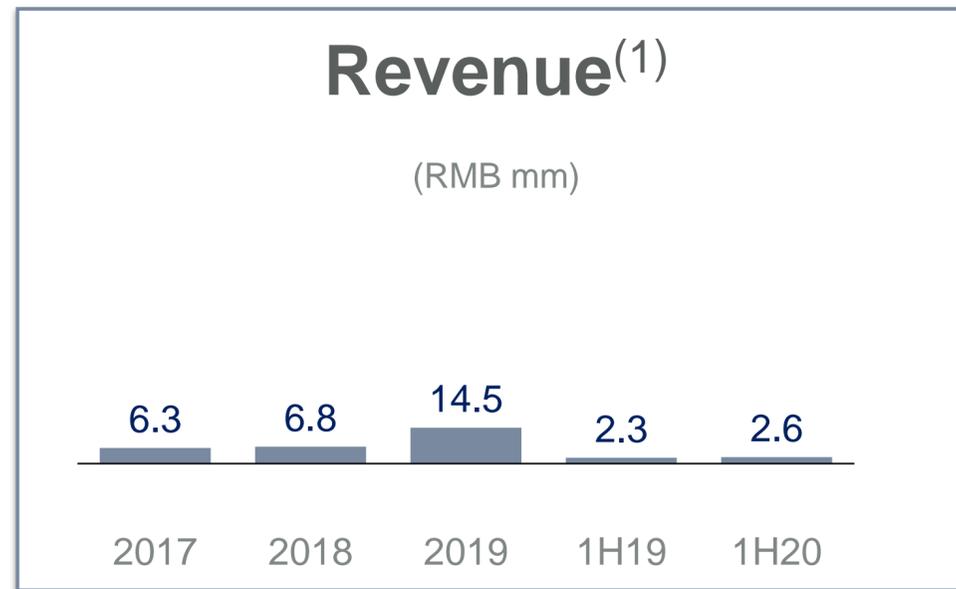
Fruquintinib  
Surufatinib  
2 FTDs



HTD1801  
2 FTDs



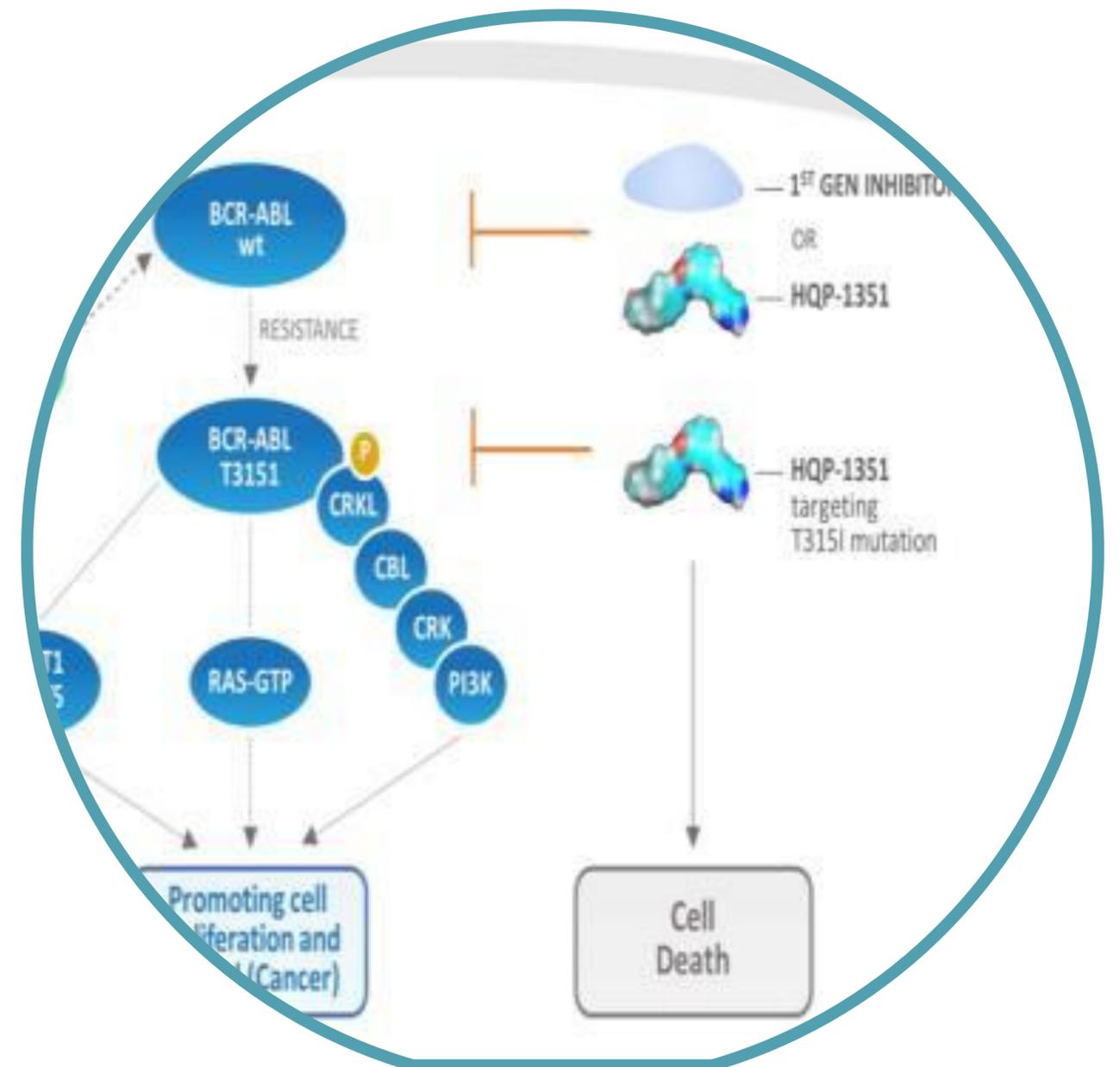
# Key Financial Highlights



1) its revenue from provision of research and development services, and compounds library and intellectual property license fee income; 2) EBIT = Gross Profit – R&D Expense – Other OPEX 3) Cash & Equivalents include cash and bank balances, and other financial assets, which represent mainly investment in short-term financial productsThe group derives

# HQP1351 Olverembatinib Overview

3<sup>rd</sup> Gen BCR-ABL/KIT  
Multi-kinase Inhibitor



# Huge Unmet Medical Needs in CML

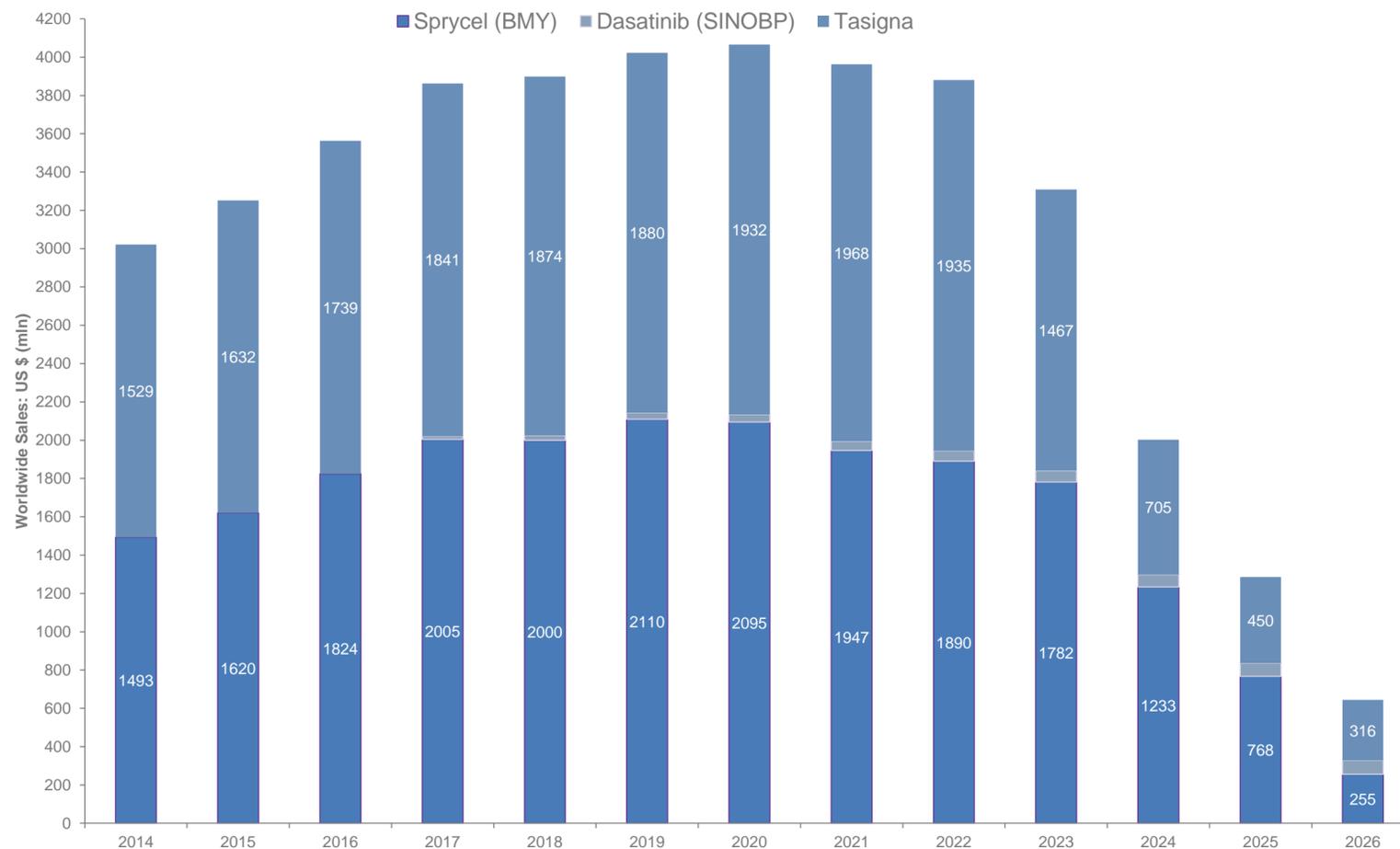
- Though TKIs have revolutionized management of CML, many patients develop resistance or intolerance to available TKIs;
  - **1<sup>st</sup> gen TKI Imatinib:** Fails in up to 40% of patients due to BCR-ABL1 resistant mutations, intolerance, and/or suboptimal adherence to therapy schedule.
    - One of the most frequent BCR-ABL mutations is T315I, ranging from 5 to 25% of CML cases
    - Only 50% of resistant patients achieve a durable CCR or deeper response if they are switched to dasatinib, nilotinib, bosutinib, or ponatinib <sup>1,2</sup>
  - **2<sup>nd</sup> gen TKIs (dasatinib and nilotinib):** Fail in high number of patients due to T315I or other mutations. Treatment failure with 2<sup>nd</sup> gen TKIs portends a poor prognosis among the estimated 37%-52% of patients<sup>3</sup>
  - **The only 3<sup>rd</sup> gen TKI Ponatinib:** the ONLY TKI able to overcome T315I mutation. It received Black box warnings of cardiovascular events.
- None of the above TKIs are effective in the presence of some “compound” mutations.

HQP1351: **Effective** in BCR-ABL Wild Type as well as T315I mutation,

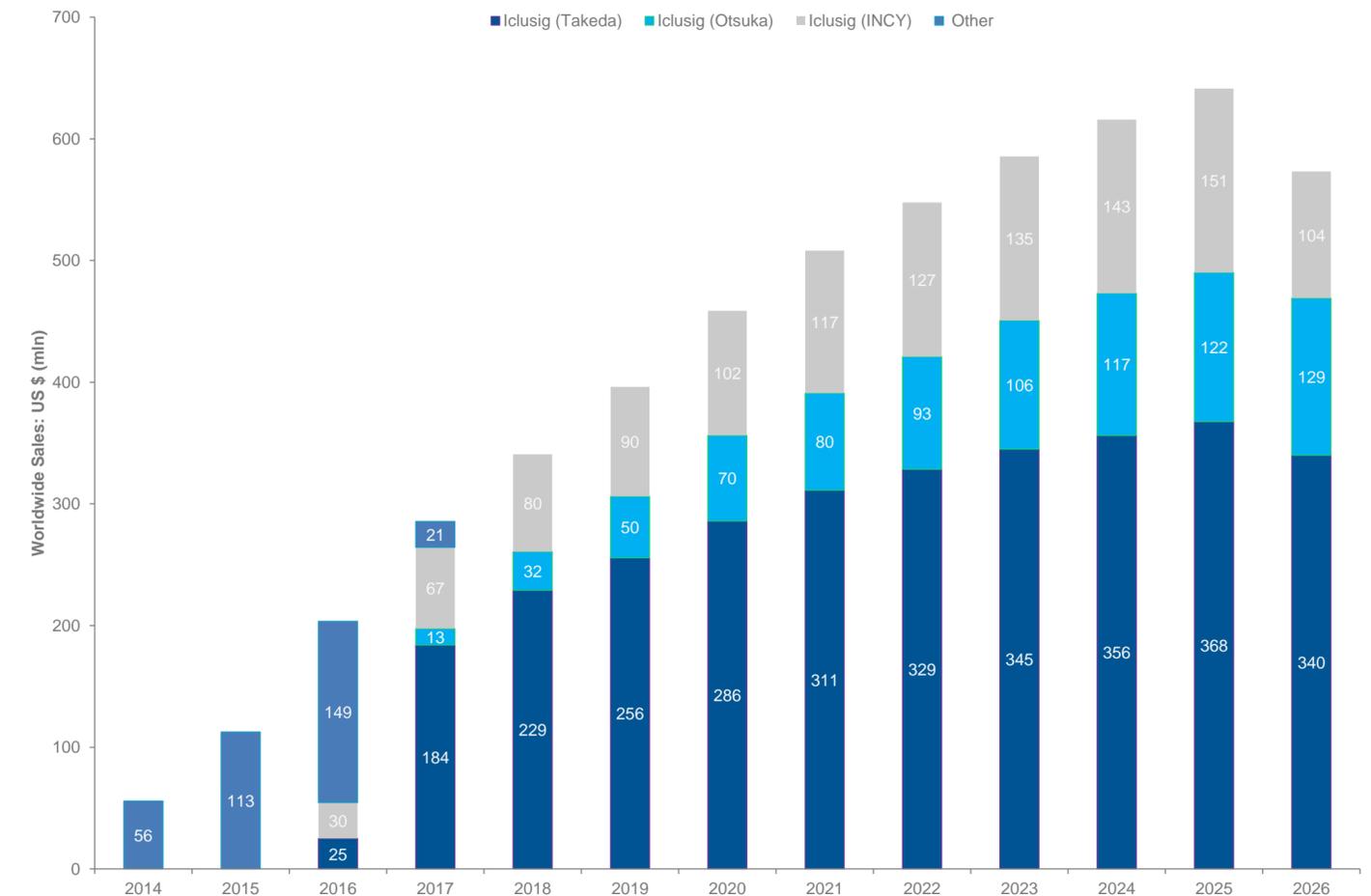
**First** 3rd generation BCR-ABLTKI developed in China, only **Second** in the entire world

# Large Potential Market for 3rd Gen BCR-ABL Inhibitors

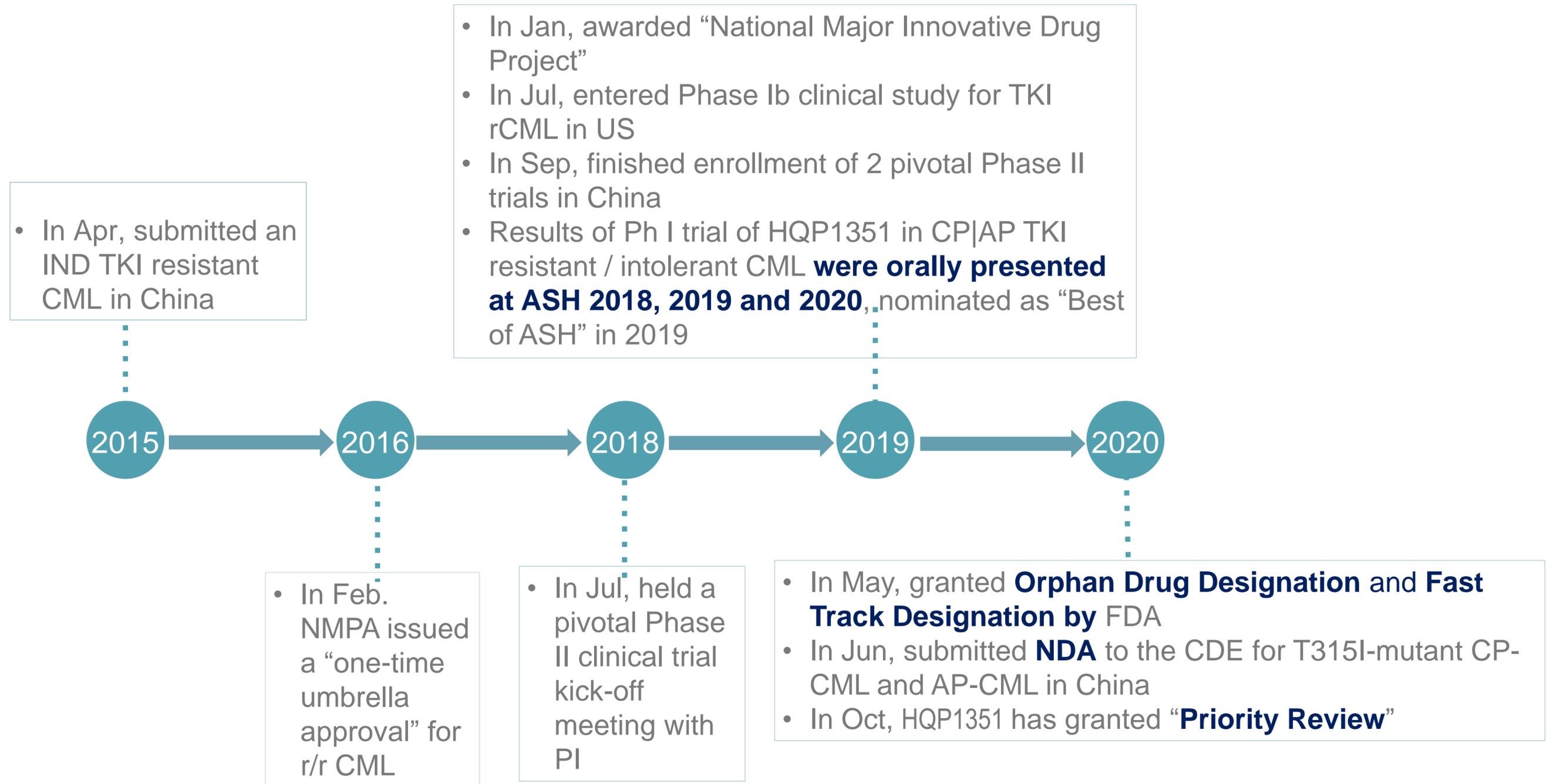
Global sales of dasatinib and nilotinib peaked at \$4,066M in 2020



Global sales of ponatinib forecasted at \$641M in 2025



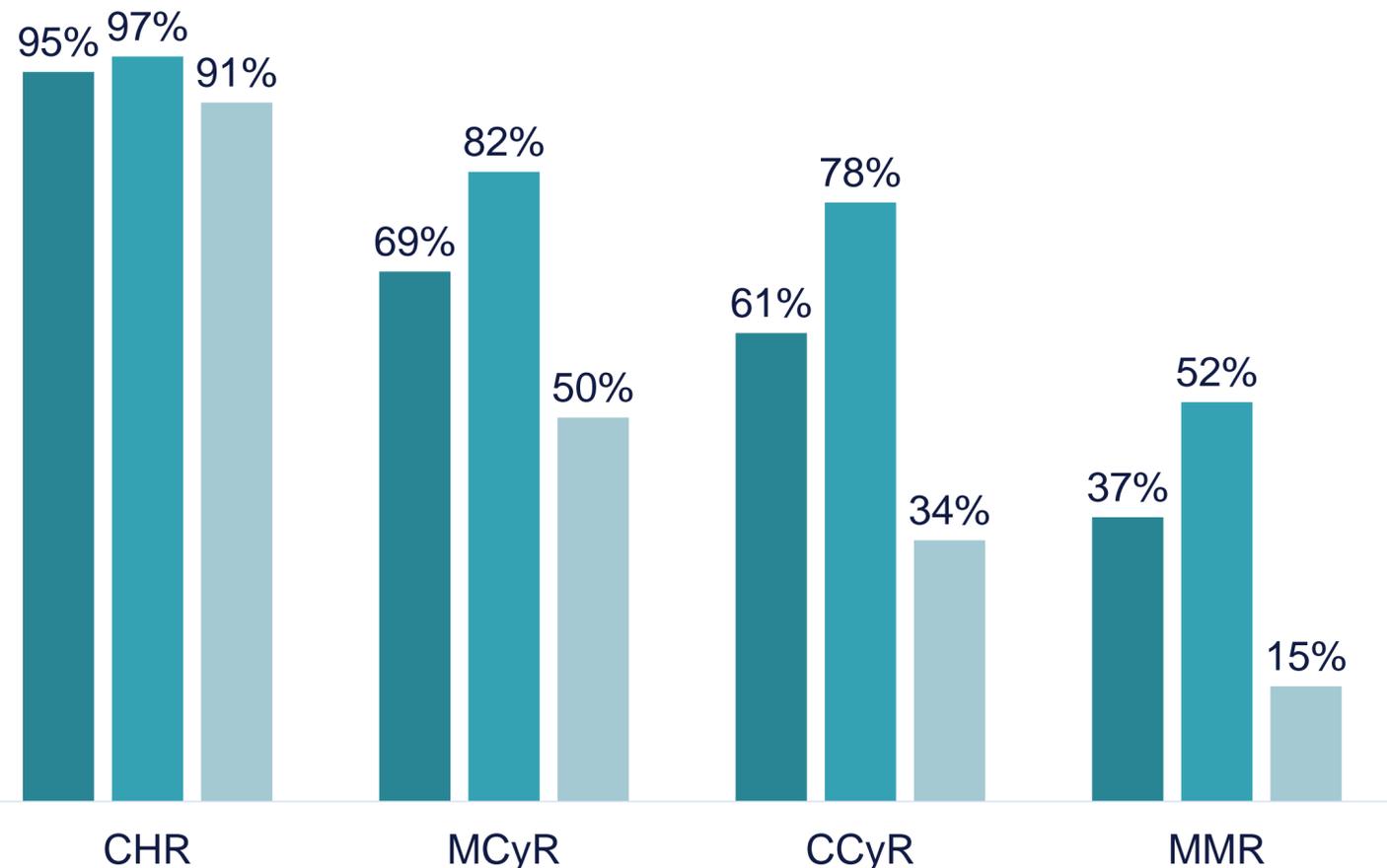
# Development Milestone: From IND Approval to NDA in 4 Years



# Phase I Study: Highly Efficacious in TKI Resistant CML Patients

CP

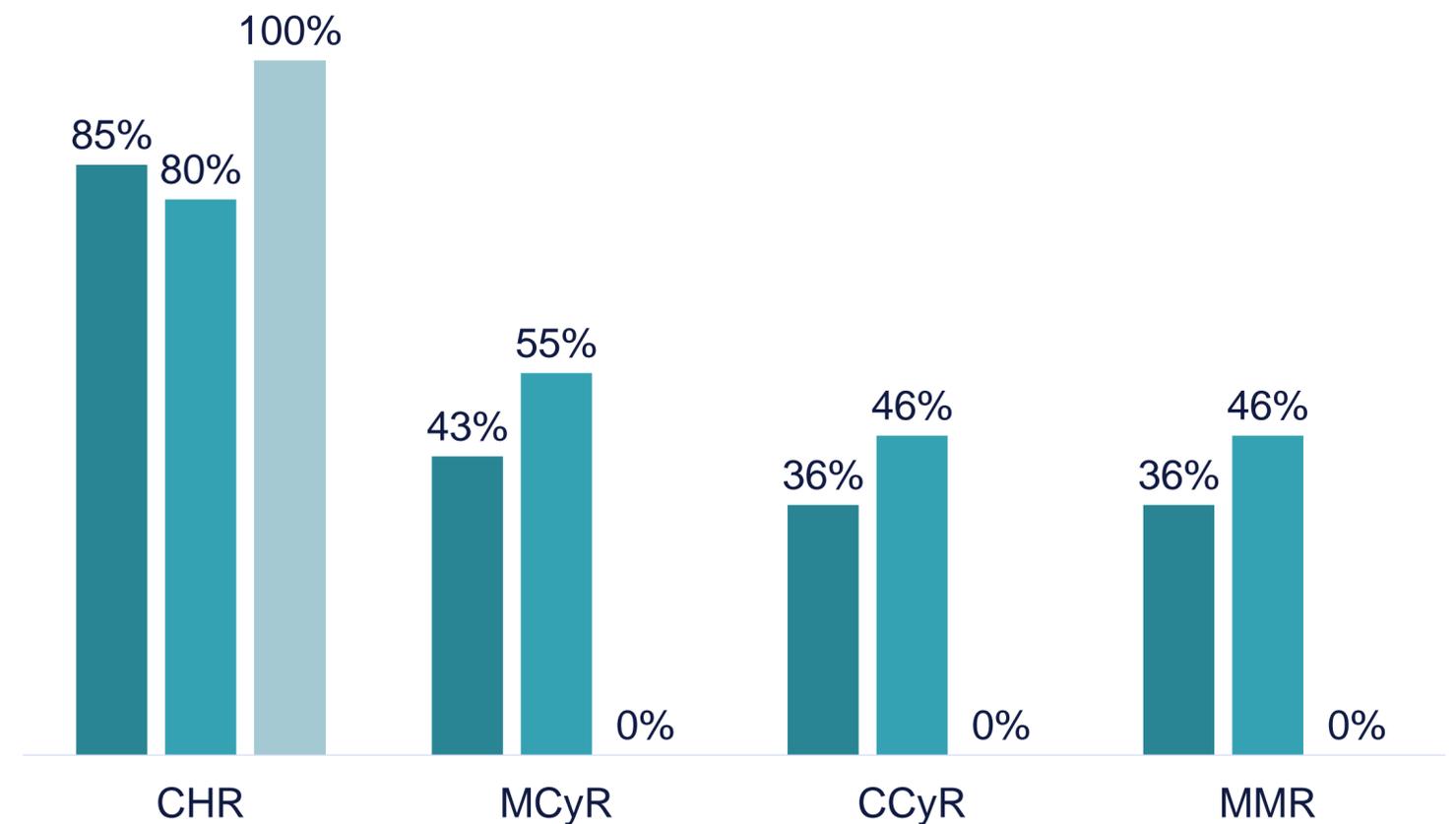
■ Total n=87 ■ T315I+ n=52 ■ T315I- n=35



CML Response Criteria: Complete Hematological Response(CHR),  
Bone Marrow; Major Cytogenic Response (MCyR\*) Complete Cytogenic Response (CCyR),  
 Major Molecular Response (MMR<sup>^</sup>) | \* MCyR is a validated End Point, ^ MMR defined by PCR (<1/1000)

AP

■ Total n=14 ■ T315I+ n=11 ■ T315I- n=3



CML Response Criteria: Complete Hematological Response(CHR),  
Bone Marrow; Major Cytogenic Response (MCyR\*) Complete Cytogenic Response (CCyR),  
 Major Molecular Response (MMR<sup>^</sup>) | \* MCyR is a validated End Point, ^ MMR defined by PCR (<1/1000)

# Well-Tolerated With Minimal Dose Interruptions

## Long Duration of Treatments

- Longest duration of treatment is **50 months**
- The average observation period for the Ph I clinical trial is more than **2 years**; mean exposure **30.0 months**, median exposure **30.8 months**
- **20 patients'** duration of treatment more than **3 years**
- **66 patients'** duration of treatment between **2 - 3 years**.

## Minimal Discontinuation

- Among 101 patients enrolled, **82 patients** remains on the study up-to-date ( since 2016 )
- Discontinuation:
- **19 patients** discontinued treatment due to AE
  - **8 patients** due to PD
  - **5 patients** due to AE,
  - **6 patients** due to other reasons

## Low Cardiovascular AE

- Much lower cardiovascular events reported; no fatal myocardial infarction or stroke was reported, compared to serious arterial occlusion events (AOEs) observed in 35% of ponatinib treated patients in clinical trials

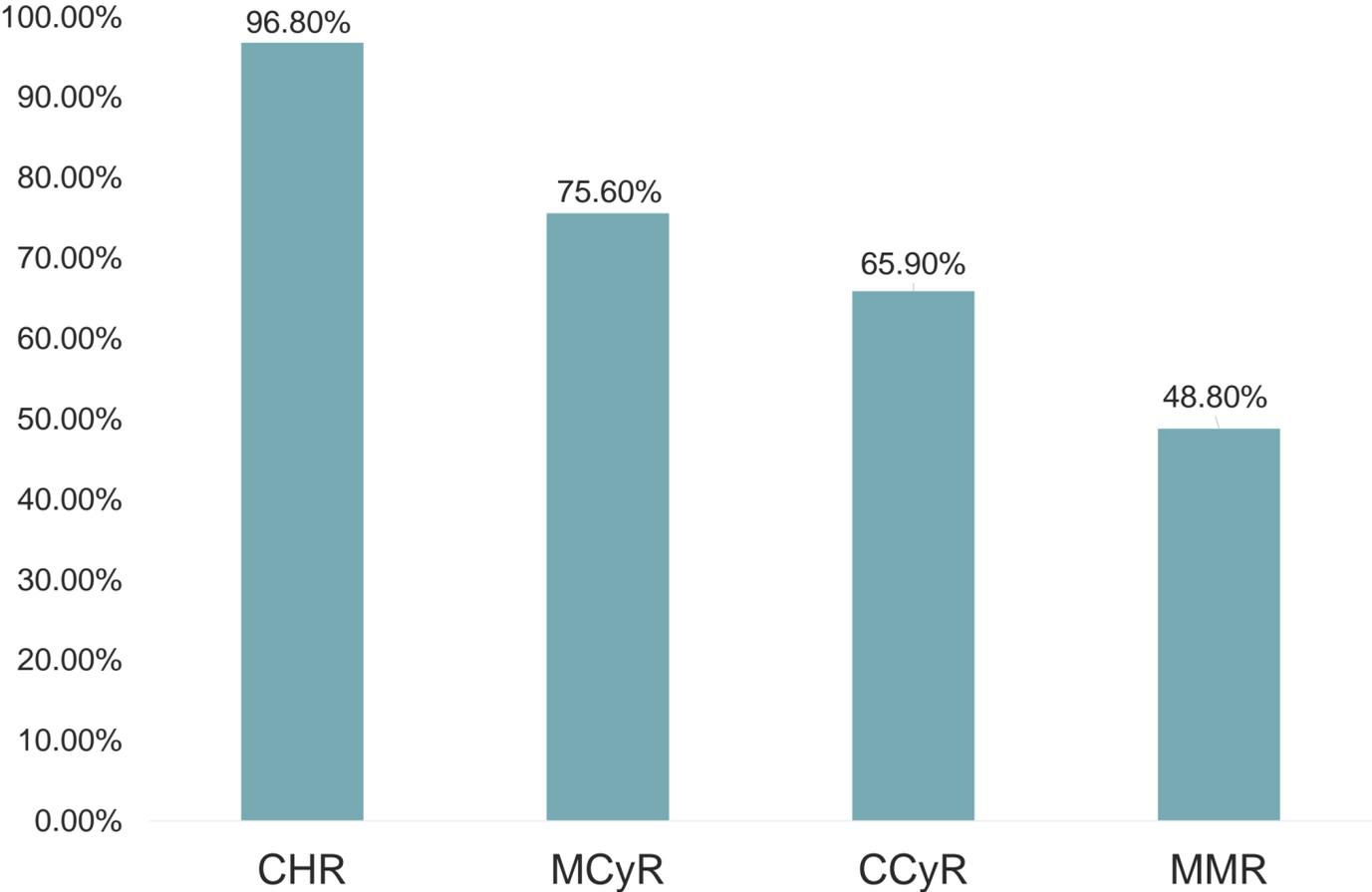
## Rare Liver Toxicity

The liver toxicity was rarely reported and was mild or moderate, compared to ALT or AST elevation observed in 56% (all grade) and 8% (grade 3 or 4) of patients treated with ponatinib

# Pivotal Ph II Study: Highly Efficacious in T315I-Mutated CML Patients

## CML-CP

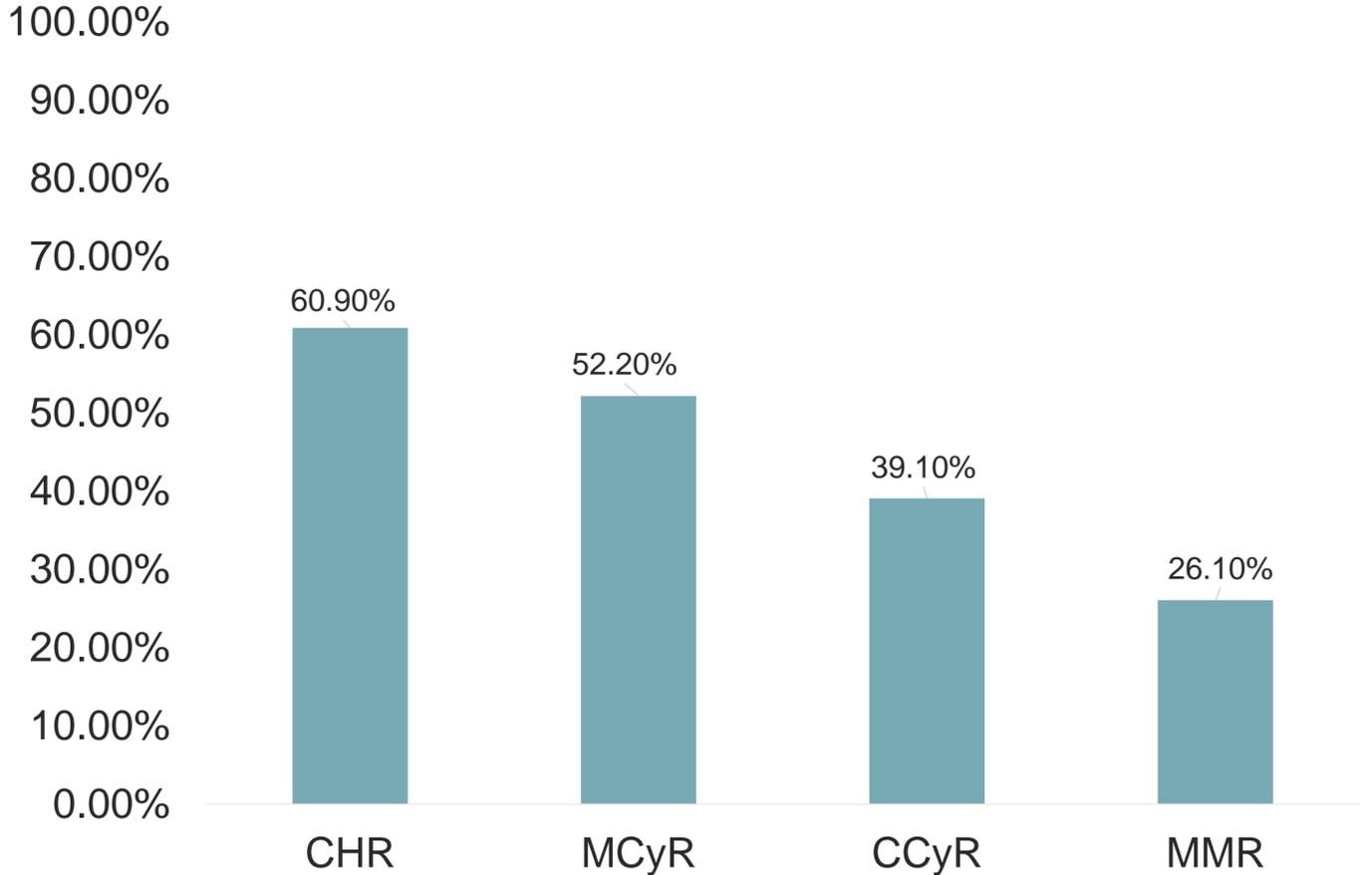
T315I+n=41



CML Response Criteria: Complete Hematological Response(CHR), Bone Marrow; Major Cytogenic Response (MCyR\*) Complete Cytogenic Response (CCyR), Major Molecular Response (MMR^<sup>^</sup>) | \* MCyR is a validated End Point, ^ MMR defined by PCR (<1/1000)

## CML-AP

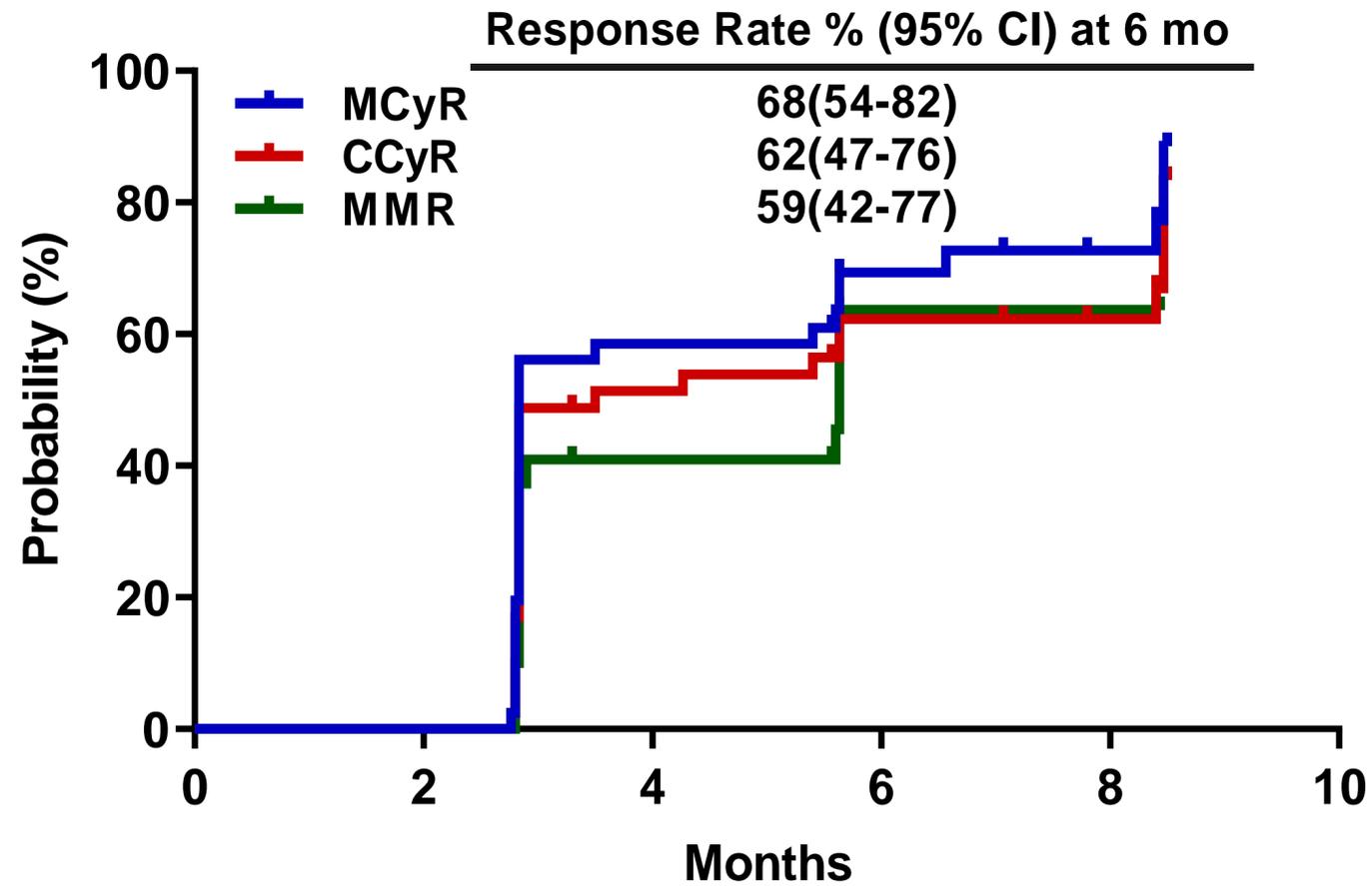
T315I+n=23



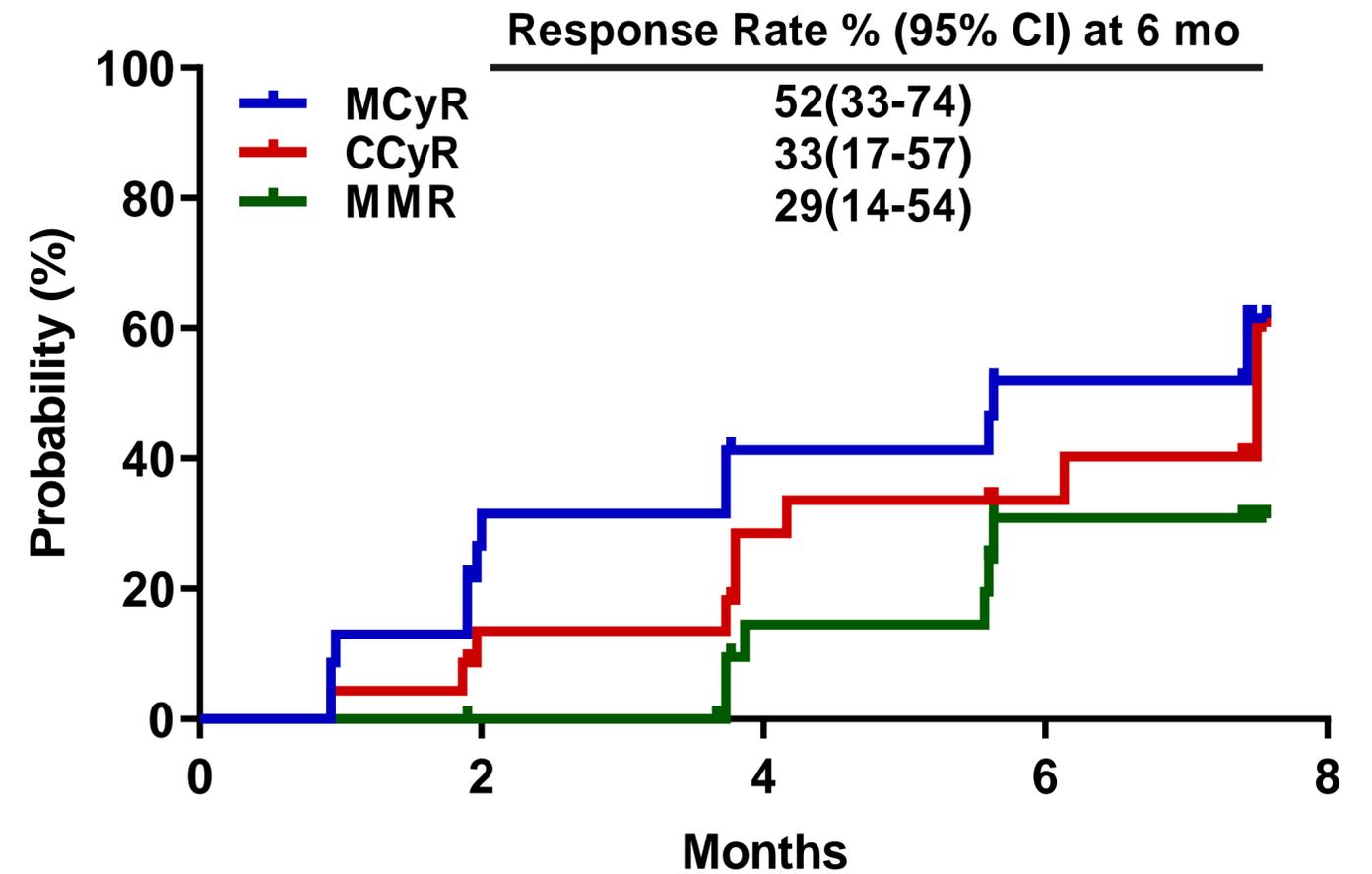
CML Response Criteria: Complete Hematological Response(CHR), Bone Marrow; Major Cytogenic Response (MCyR\*) Complete Cytogenic Response (CCyR), Major Molecular Response (MMR^<sup>^</sup>) | \* MCyR is a validated End Point, ^ MMR defined by PCR (<1/1000)

# Cumulative Incidence of Responses

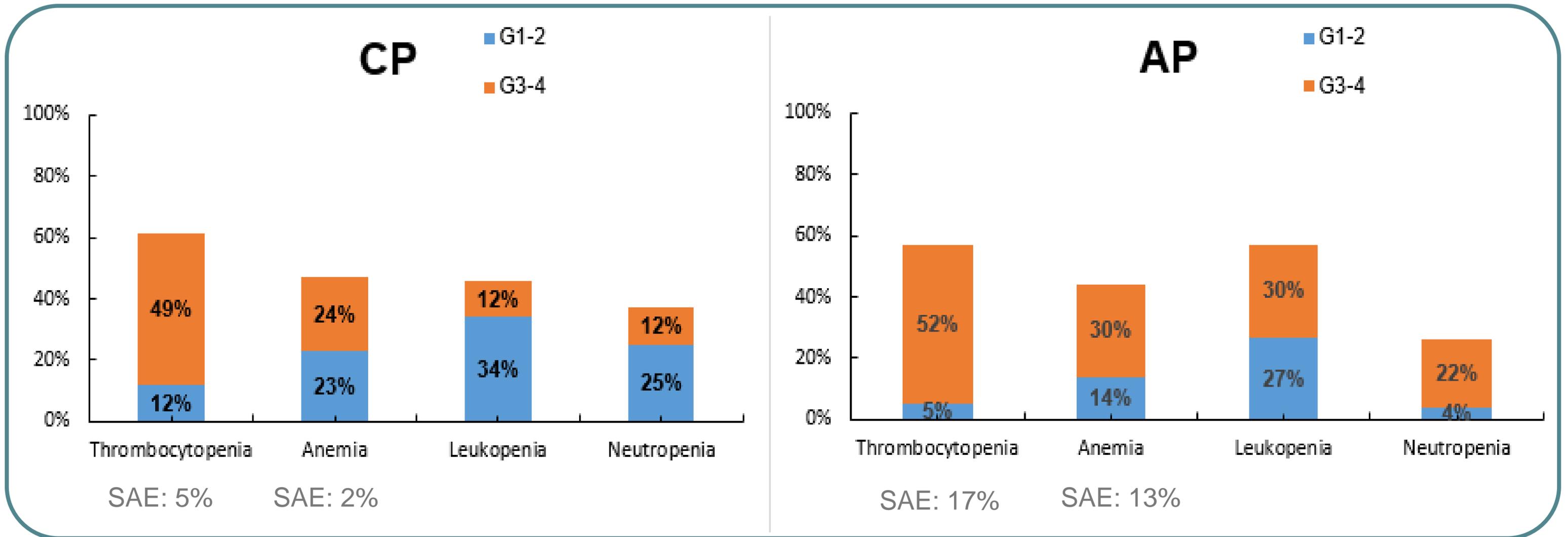
## CML-CP



## CML-AP



# Treatment-related Hematologic Adverse Events

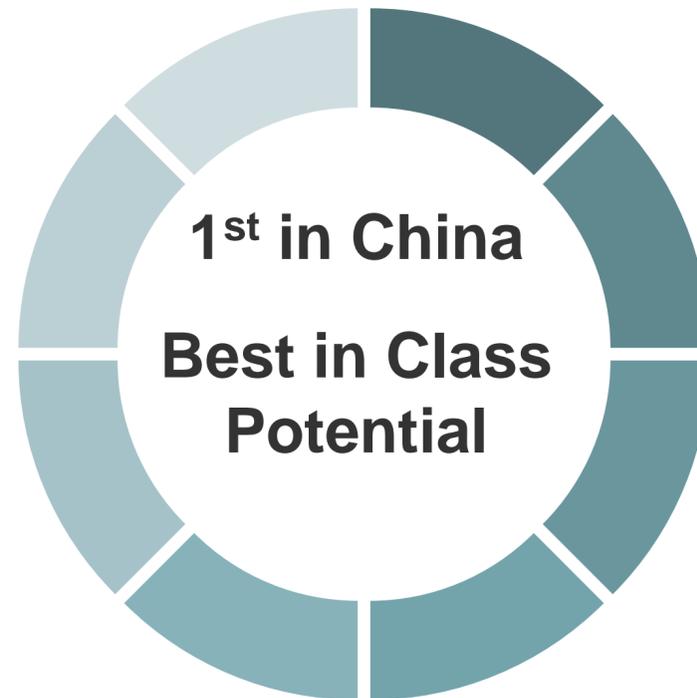


# HQP1351: T315I and Beyond

First 3<sup>rd</sup> generation of BCR-ABL TKI being developed in China

NDA was submitted to CDE as planned on June 15 in China, grant with “Priority review”

Potentially better tolerance than Ponatinib based on 300+ subjects treated with HQP1351



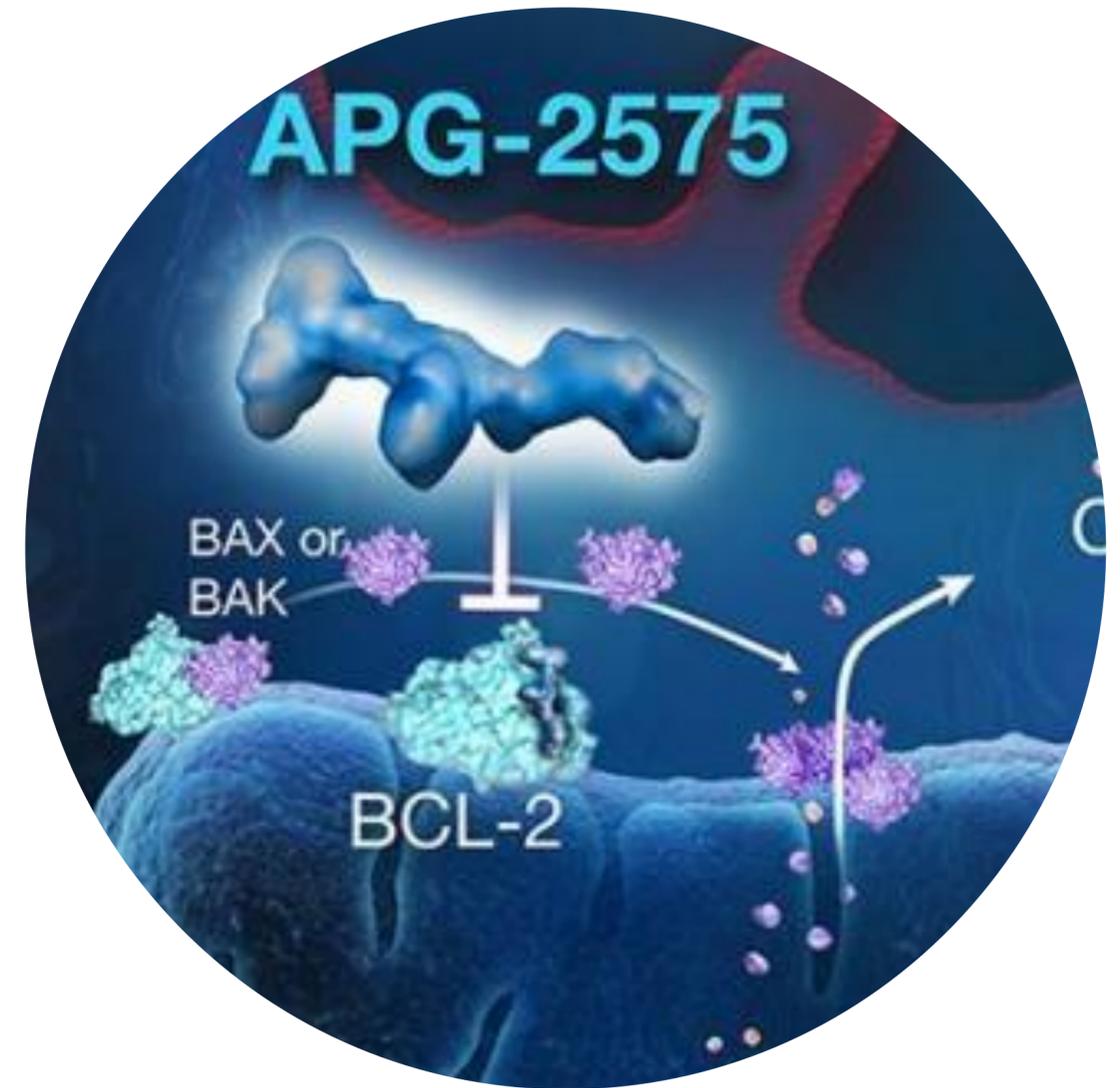
Ph II pivotal studies in patients with TKI resistant BP-CML, Ph+ ALL

Efficacious on the patients who failed/intolerant to ponatinib. Also active in the presence of compound mutations where ponatinib is ineffective.

Proposed Phase II pivotal study in US focus on the CML Pts with R/R ponatinib or multiple / compound mutations

# APG-2575 Overview

Novel, orally administered Bcl-2 selective inhibitor, follow to Venclexta®



# BCL-2 is a Validated Target

## BCL-2 inhibitor



- Tumor cells may become dependent on Bcl-2 for survival
- Inhibiting Bcl-2 releases pro-apoptotic proteins, which trigger apoptosis through the apoptosome

Bcl-2 Selective Inhibitors		
		
Compound	APG-2575	Venetoclax (ABT-199)
MOA	Orally available and Bcl-2 selective inhibitor	Orally available and Bcl-2 selective inhibitor
Clinical stage	Ph Ib/II	Marketed (CLL, AML)
Indication	CLL, AML, WM, MM, T-PLL	CLL, AML, MM, MCL, MDS, NHL, ALL, Breast cancer, Prostate cancer
Combo agents	BTK, CD20, MDM2, BCR-ABL TKI	BTK, CD20, CDK9, Pi3K, MDM2, JAK, PD-(L)1, FLT-3, IDH, CD33, CD38, etc.
Comments	<ul style="list-style-type: none"> <li>• Patient-friendly daily dose-ramp-up</li> <li>• No or Low TLS</li> <li>• Less risk DDI</li> <li>• Less neutropenia likely</li> <li>• Strong synergy with in-house MDM2-p53 inhibitor APG-115</li> <li>• Plan to focus on the China market</li> </ul>	<ul style="list-style-type: none"> <li>• NDA approved in April 2016</li> <li>• First-in-class Bcl-2 inhibitor</li> <li>• 5 FDA Breakthrough Therapy designations</li> <li>• 4 approved indications across CLL and AML populations</li> <li>• 250+ trials across US, China, EU, Japan, etc.</li> <li>• Enrolled 10,000+ patients</li> </ul>

# Clinical POC Established

More than **100 subjects** have been enrolled into the APG-2575 studies, including R/R CLL , FL , MCL, DLBCL, WM, MM, AML and HCL patients, dosed ranging from 20mg to 1200mg

**Proof of concept established** in CLL, more than 30 pts enrolled, 70% evaluated achieved PR

**Potentially more tolerable than Venetoclax:** no TLS, no DLT, no MTD reported

**4 Orphan Drug Designations (ODD):** CLL,WM, MM,AML

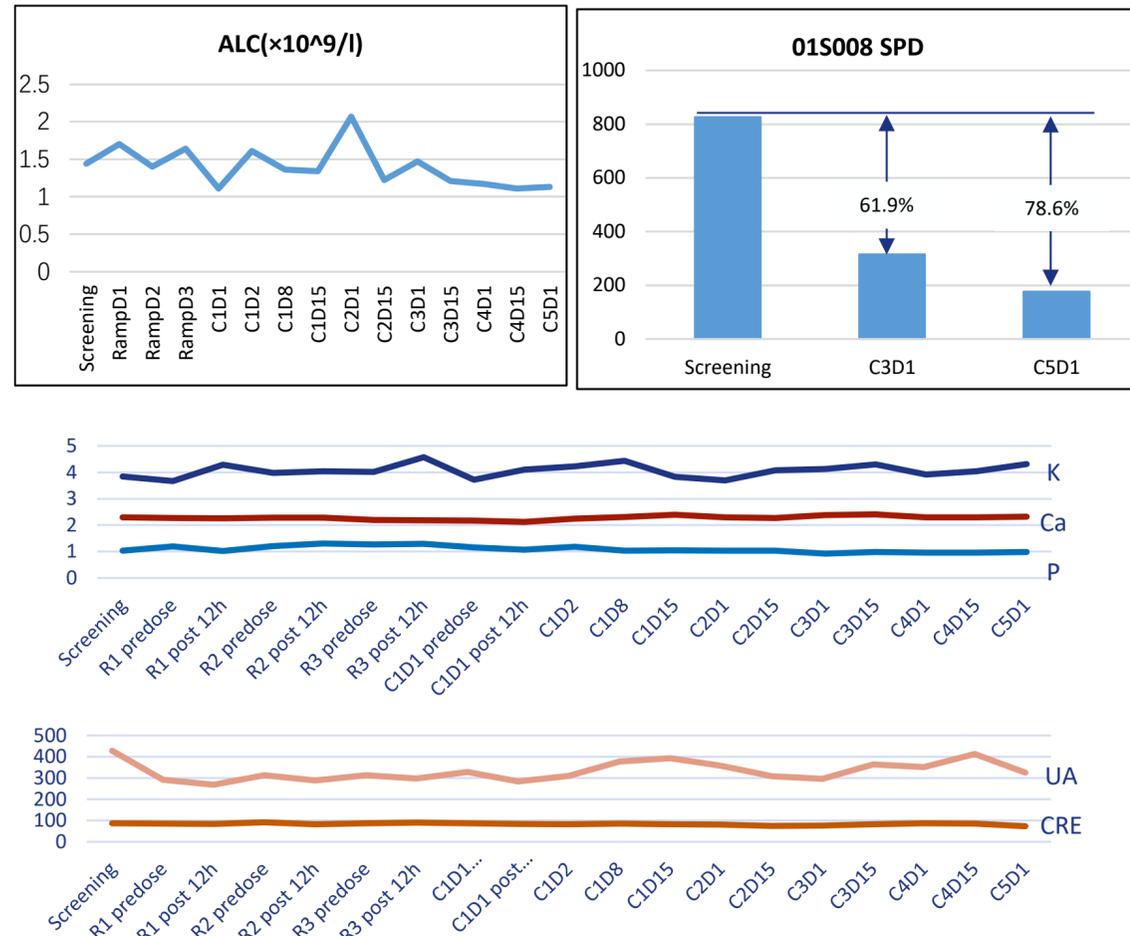
Plan to submit the protocol for treatment of patients with ER+ breast cancer and other solid tumors by Q1 2021

Plan to get CDE approval on the Phase II pivotal study design as a single agent for treatment of R/R CLL by the Q4 2021

# APG-2575-CN-001 Ph I Interim data | Activity

## Ibrutinib Resistant High Risk Patient; Rapid and Deep Response

### Patient 1S008: PR parameters

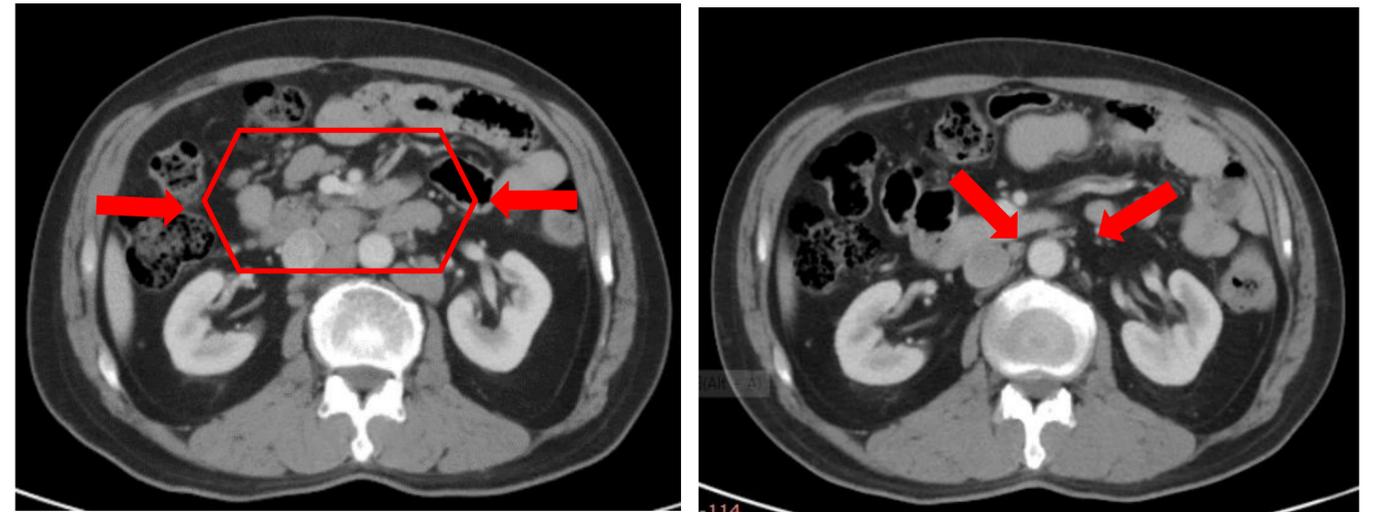


### Patient 1S008: -78.6% Nodal Response

PR in r/r CLL (IgVH mutation, no TP53)

Before APG-2575

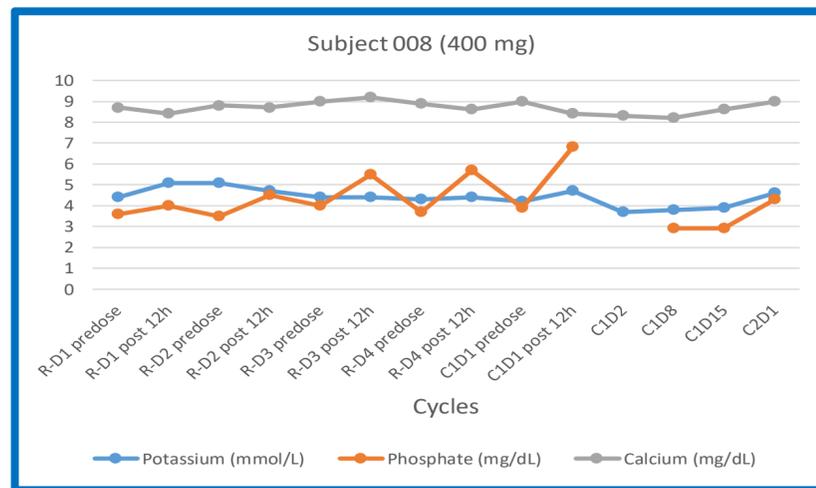
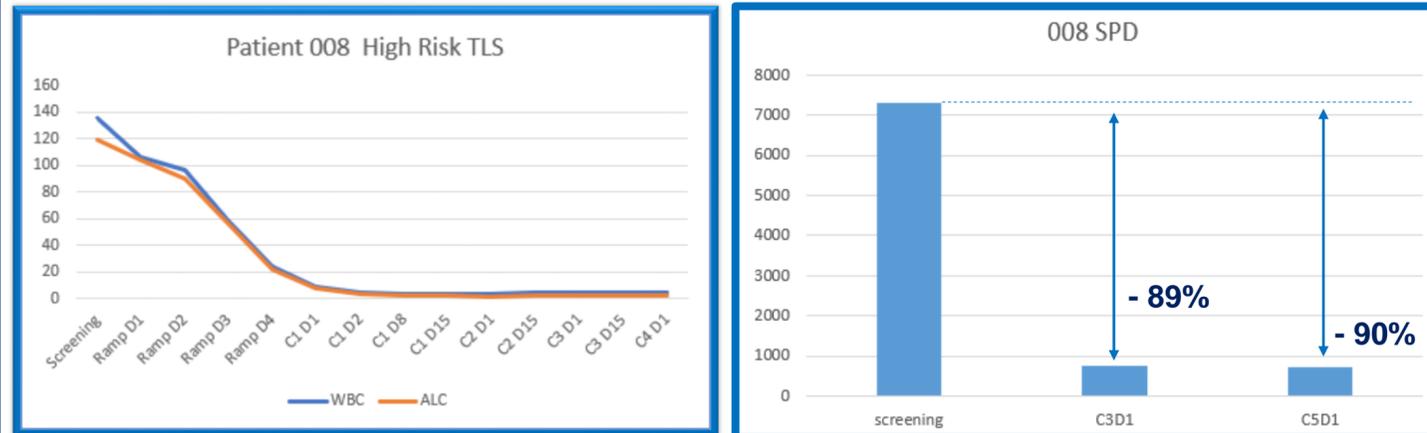
After APG-2575



Lymph Node Response: C3D1 **-62%**; C5D1 **-78.6%**

# Del17p CLL Patient at High Risk of TLS: Rapid & Deep Response

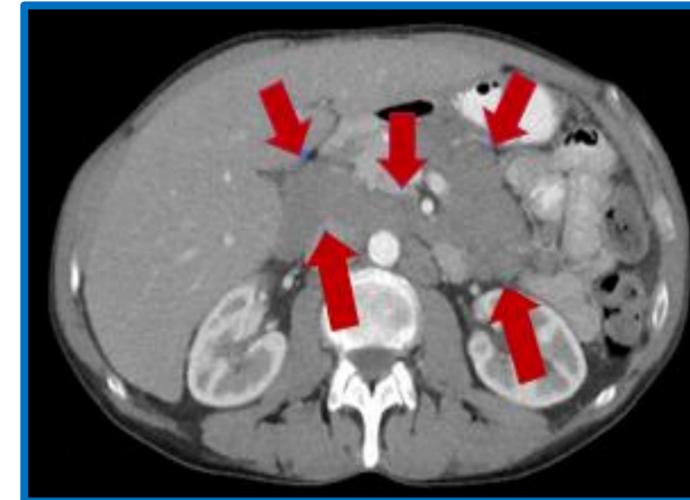
## Patient 008: PR parameters



## Patient 008: -90% Nodal Response

Durable PR in a patient with r/r CLL

Before APG-2575

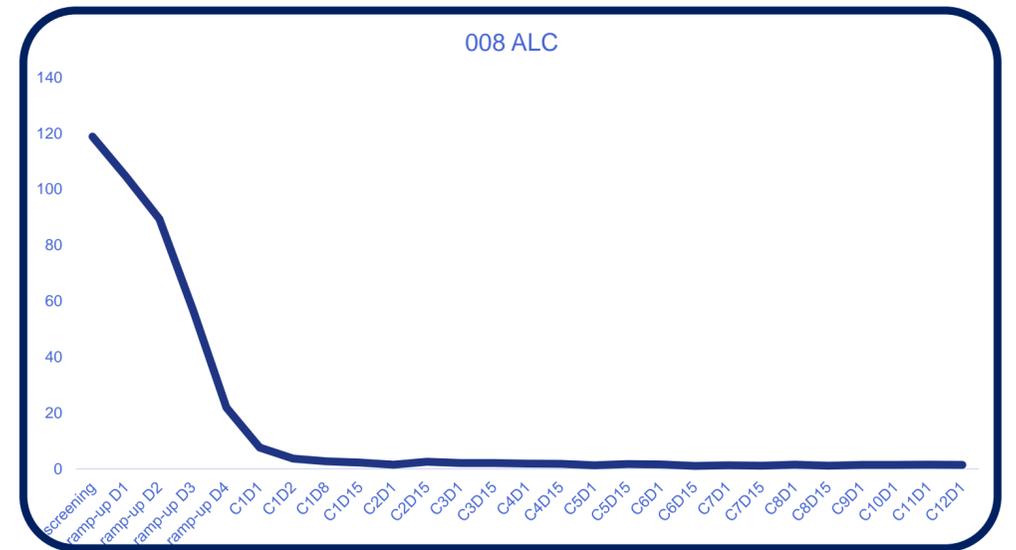
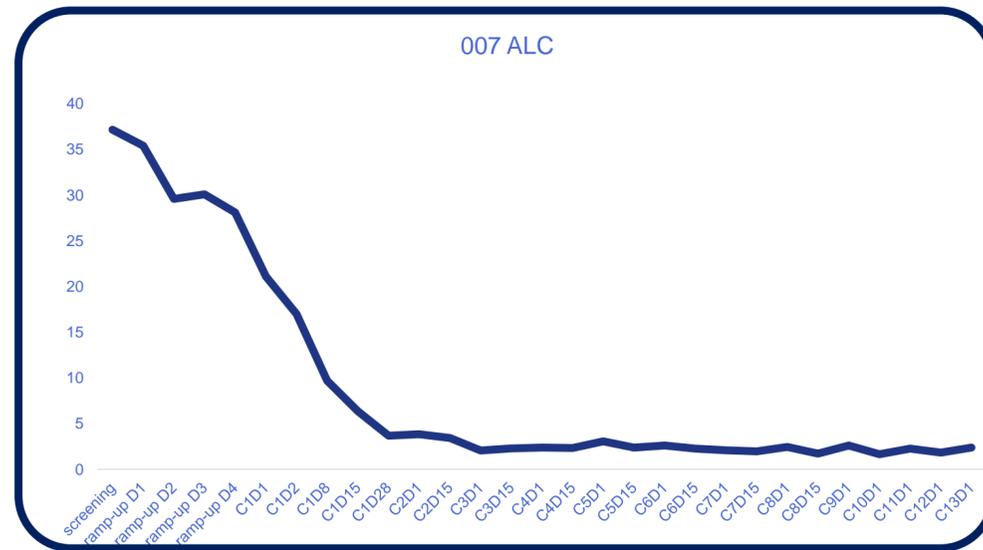
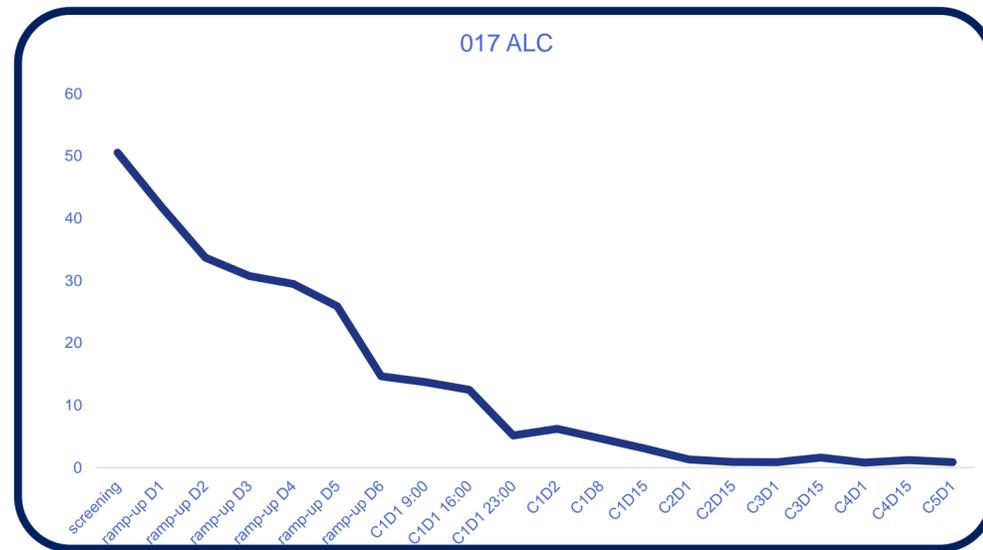


After APG-2575

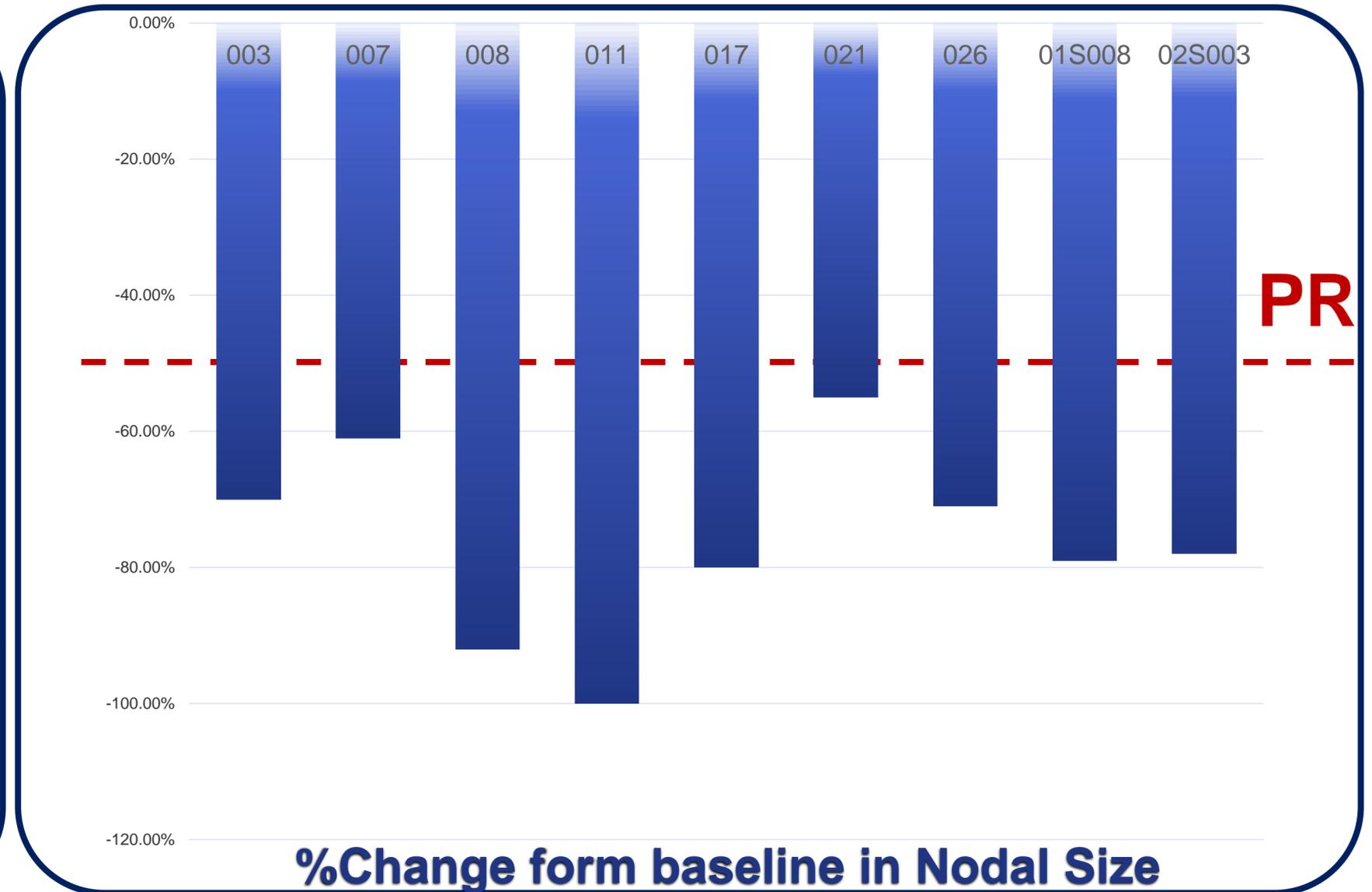
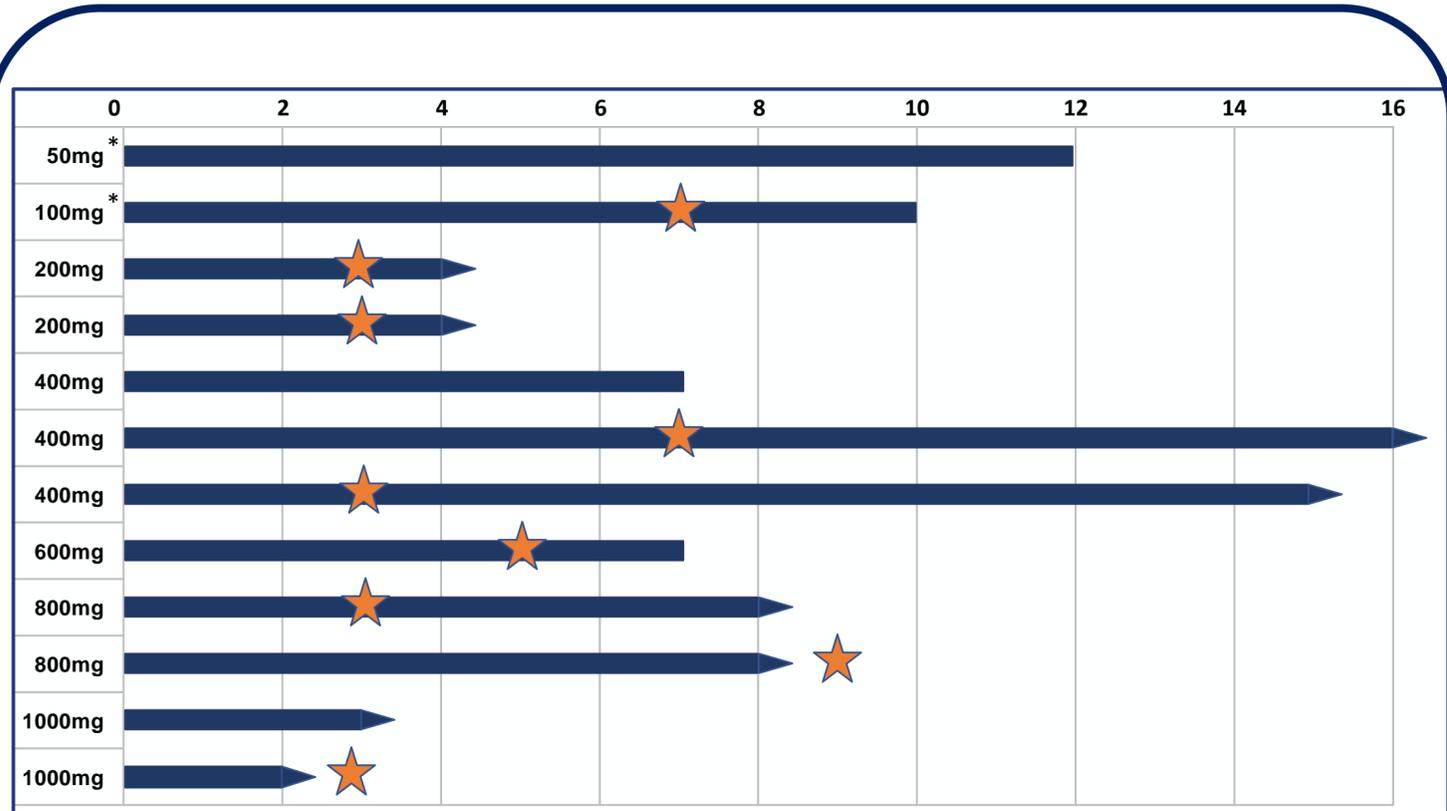


Nodal Response: C3D1-89% | C5D1-90%

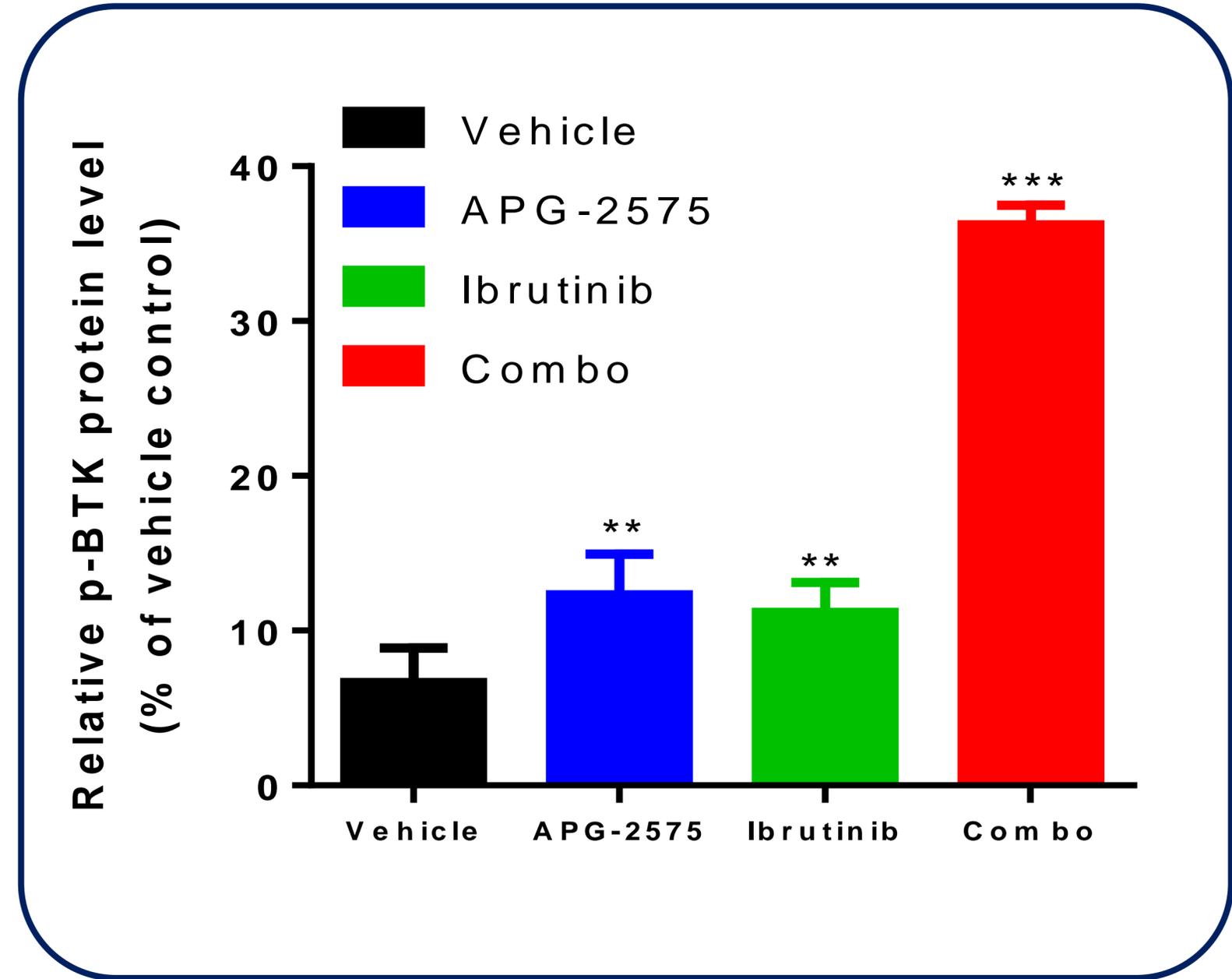
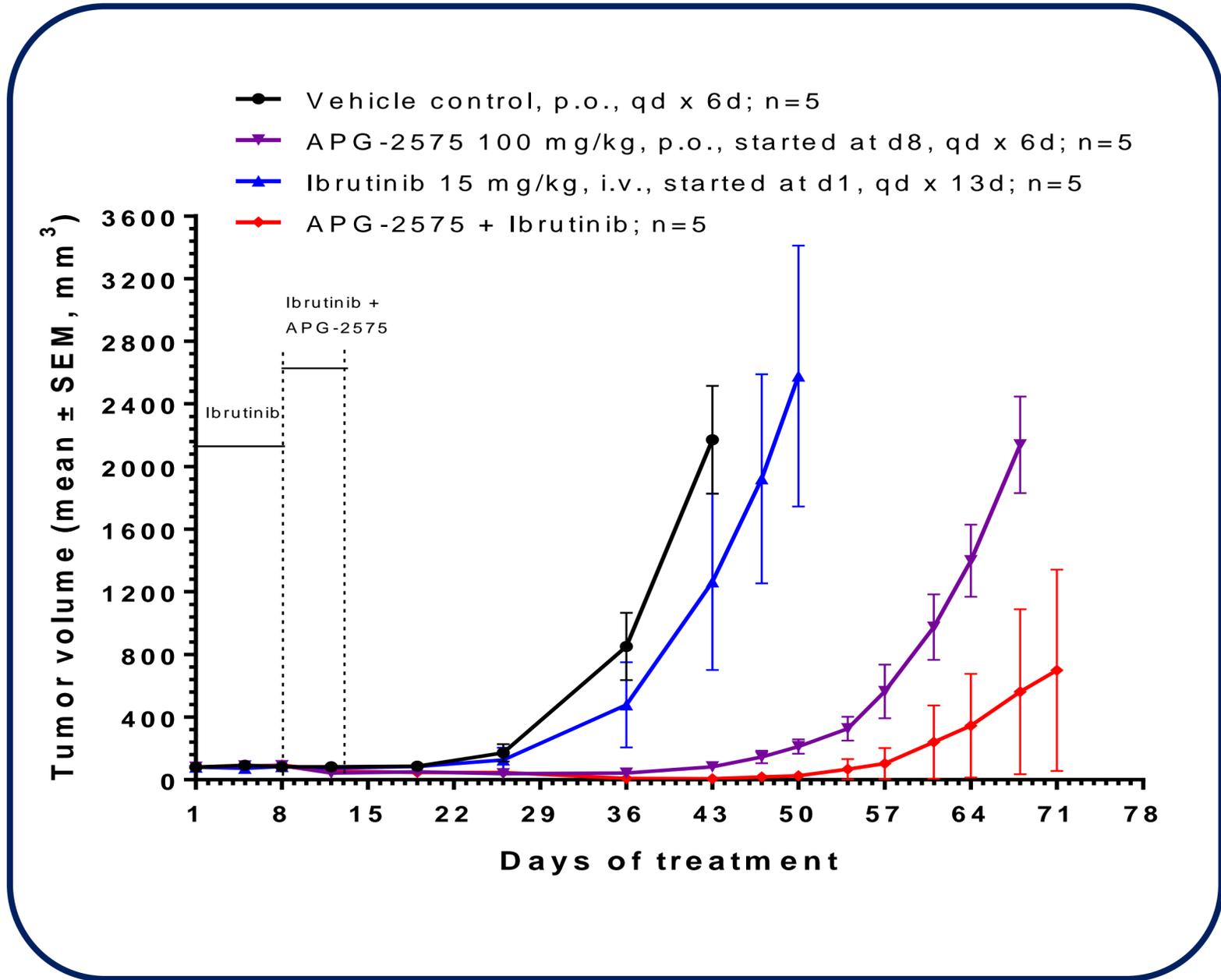
# ALC Response Kinetics in R/R CLL Patients



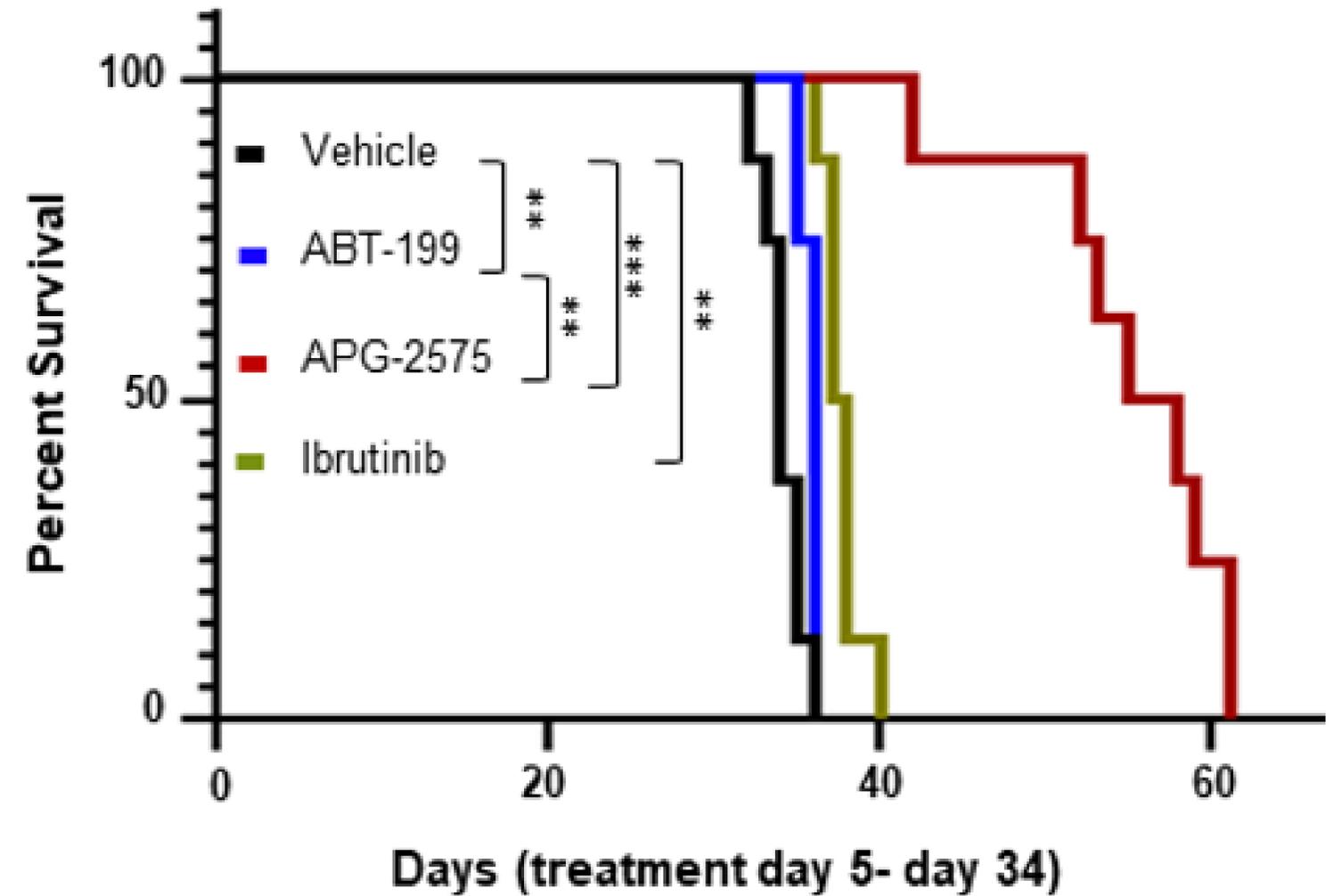
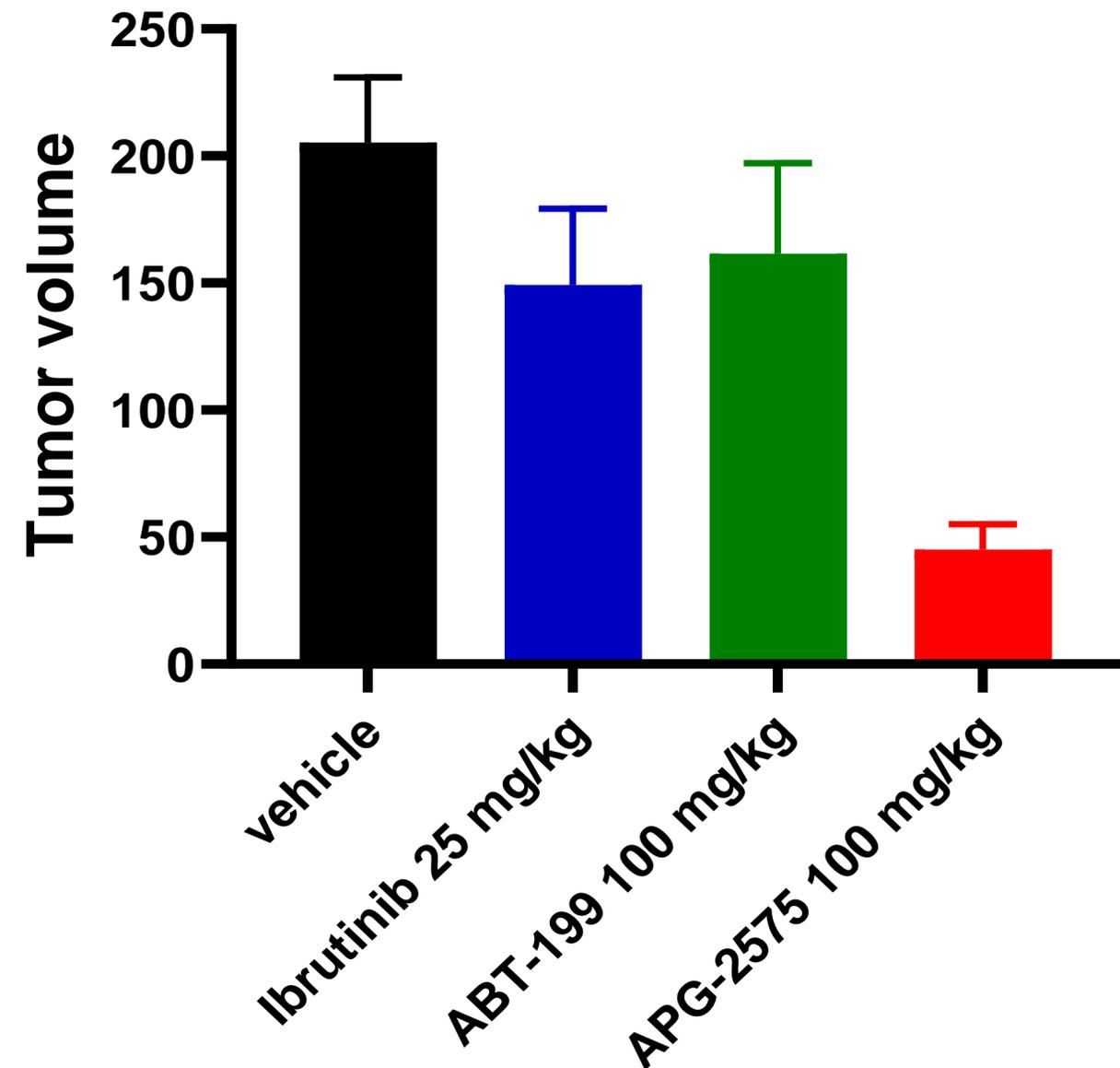
# 70% PR in Evaluable R/R CLL/SLL Patients



# Synergistic Effects of APG-2575 in Combination with Ibrutinib



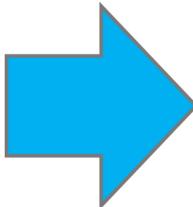
# Efficacious In BTK Resistant WM PDX Model In Which Venetoclax Shows NO Activity



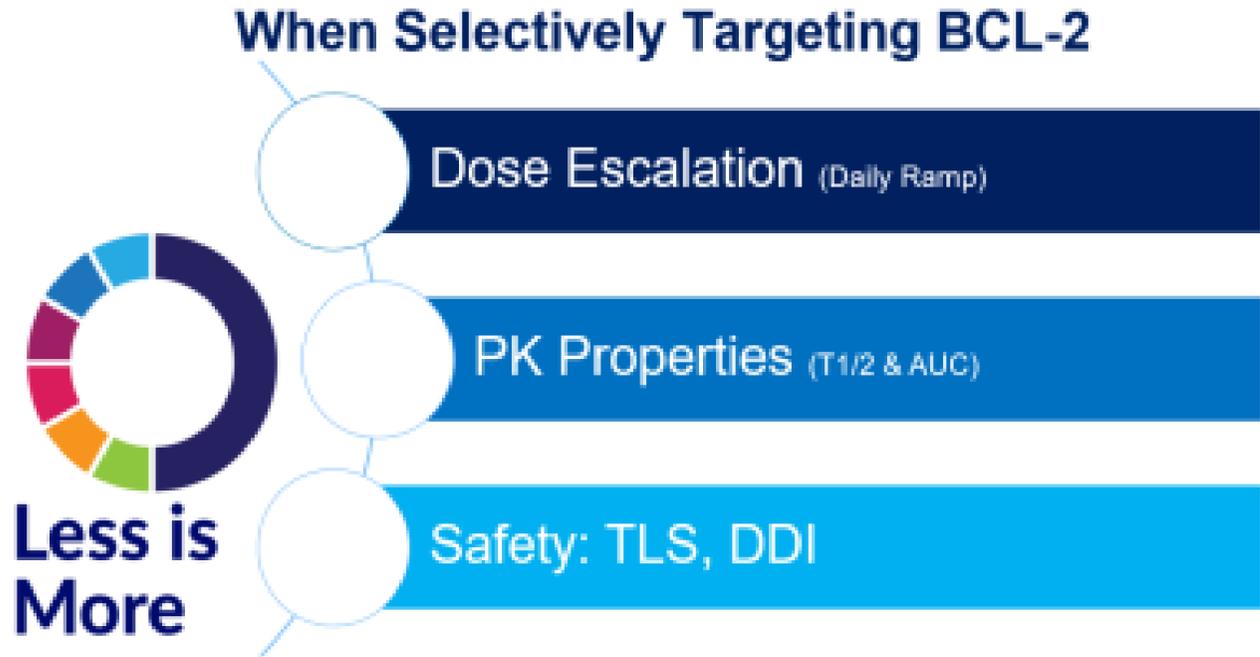
# APG-2575 and Venetoclax

## Differences Compared to Venetoclax:

- Efficacious in BTK resistant WM PDX model in which Venetoclax shows no effect
- Daily Ramp-up verse weekly ramp up
- No Clinical TLS, Lab TLS
- Short T1/2 & AUC--potentially lower risk of TLS with better tolerance profile
- Preliminary results suggest better tolerance: less neutropenia and thrombocytopenia



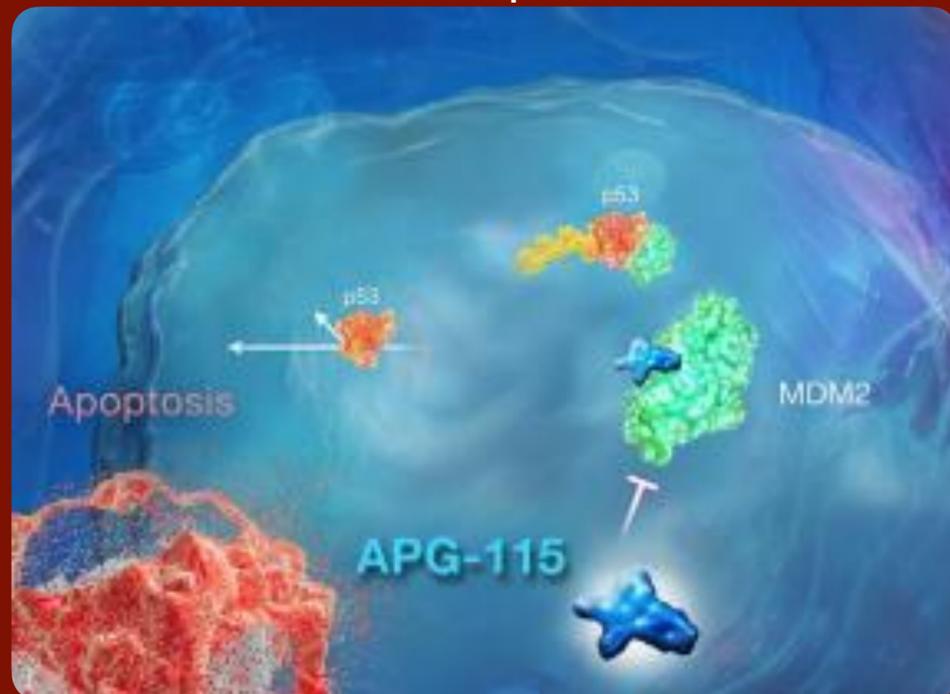
## Conclusion:



# APG-115 Overview

MDM2-p53 Inhibitor

Activates p53 tumor suppression  
via MDM2-p53 PPI



## Milestones & Developments

- Granted **ODD** for the treatment of AML, gastric cancer and soft tissue sarcoma
- Completed Two Phase I trials (U.S. & China) in advanced solid tumors or lymphoma
- U.S.: Completed enrollment of the Ph Ib clinical trial in combination with KEYTRUDA® (pembrolizumab) | Enrolling Ph II trial in combination with pembrolizumab in patients with IO resistant solid tumors; conducted in collaboration with MSD
- China: Enrolling Phase Ib clinical study treating patients with hematologic malignancies
- China: Phase Ib/II clinical trial for APG-115 in combination with chemotherapeutic or targeted agents for the treatment of patients with hematologic malignancies was approved by the NMPA in China in July 2019
- China: Phase Ib/II clinical trial for APG-115 in combination with PD-1/PD-L1 inhibitors for the treatment of patients with advanced liposarcoma (LPS) or other advanced solid tumors was cleared in Oct 2020
- U.S & China: Additional combination trial INDs are under development

# APG-115 : a Novel, Potent MDM2-P53 Inhibitor

Most potent MDM2 inhibitor in clinical development. Best-in-class potential

Journal of  
**Medicinal  
Chemistry**



Article

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**Discovery of 4-((3'R,4'S,5'R)-6"-Chloro-4'-(3-chloro-2-fluorophenyl)-1'-ethyl-2"-oxodispiro[cyclohexane-1,2'-pyrrolidine-3',3"-indoline]-5'-carboxamido)bicyclo[2.2.2]octane-1-carboxylic Acid (AA-115/APG-115): A Potent and Orally Active Murine Double Minute 2 (MDM2) Inhibitor in Clinical Development**

Angelo Aguilar,<sup>†</sup> Jianfeng Lu,<sup>†</sup> Liu Liu,<sup>†</sup> Ding Du,<sup>†</sup> Denzil Bernard,<sup>†</sup> Donna McEachern,<sup>†</sup> Sally Przybranowski,<sup>†</sup> Xiaoqin Li,<sup>‡</sup> Ruijuan Luo,<sup>‡</sup> Bo Wen,<sup>‡</sup> Duxin Sun,<sup>‡</sup> Hengbang Wang,<sup>§,#</sup> Jianfeng Wen,<sup>§,#</sup> Guangfeng Wang,<sup>§,#</sup> Yifan Zhai,<sup>§,#</sup> Ming Guo,<sup>§,#</sup> Dajun Yang,<sup>§,#,±</sup> and Shaomeng Wang<sup>\*,†</sup>

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<https://doi.org/10.1186/s40425-019-0750-6>

Journal for ImmunoTherapy  
of Cancer

RESEARCH ARTICLE

Open Access



**MDM2 inhibitor APG-115 synergizes with PD-1 blockade through enhancing antitumor immunity in the tumor microenvironment**

Douglas D. Fang<sup>1†</sup>, Qiuqiong Tang<sup>1†</sup>, Yanhui Kong<sup>1</sup>, Qixin Wang<sup>1</sup>, Jiaying Gu<sup>1</sup>, Xu Fang<sup>1</sup>, Peng Zou<sup>2</sup>, Tao Rong<sup>1</sup>, Jingwen Wang<sup>1</sup>, Dajun Yang<sup>1,3\*</sup> and Yifan Zhai<sup>1\*</sup>

**Blocks MDM2-P53 PPI & activates the tumor suppressor P53**

**Effectively induces apoptosis with the best-in-class potential**

**Directly regulates host immunological responses in the TME and potentially overcome IO resistance**

**Synergy with PD-1 blockade in both TP53WT and TP53MUT tumors**

**MDM2amp associated with Hyperprogression after  $\alpha$ PD1 Rx (Kato et al., 2017)**



亞盛醫藥  
Ascentage Pharma

# APG-115 US-002

## Ph Ib | Overview and Treatment

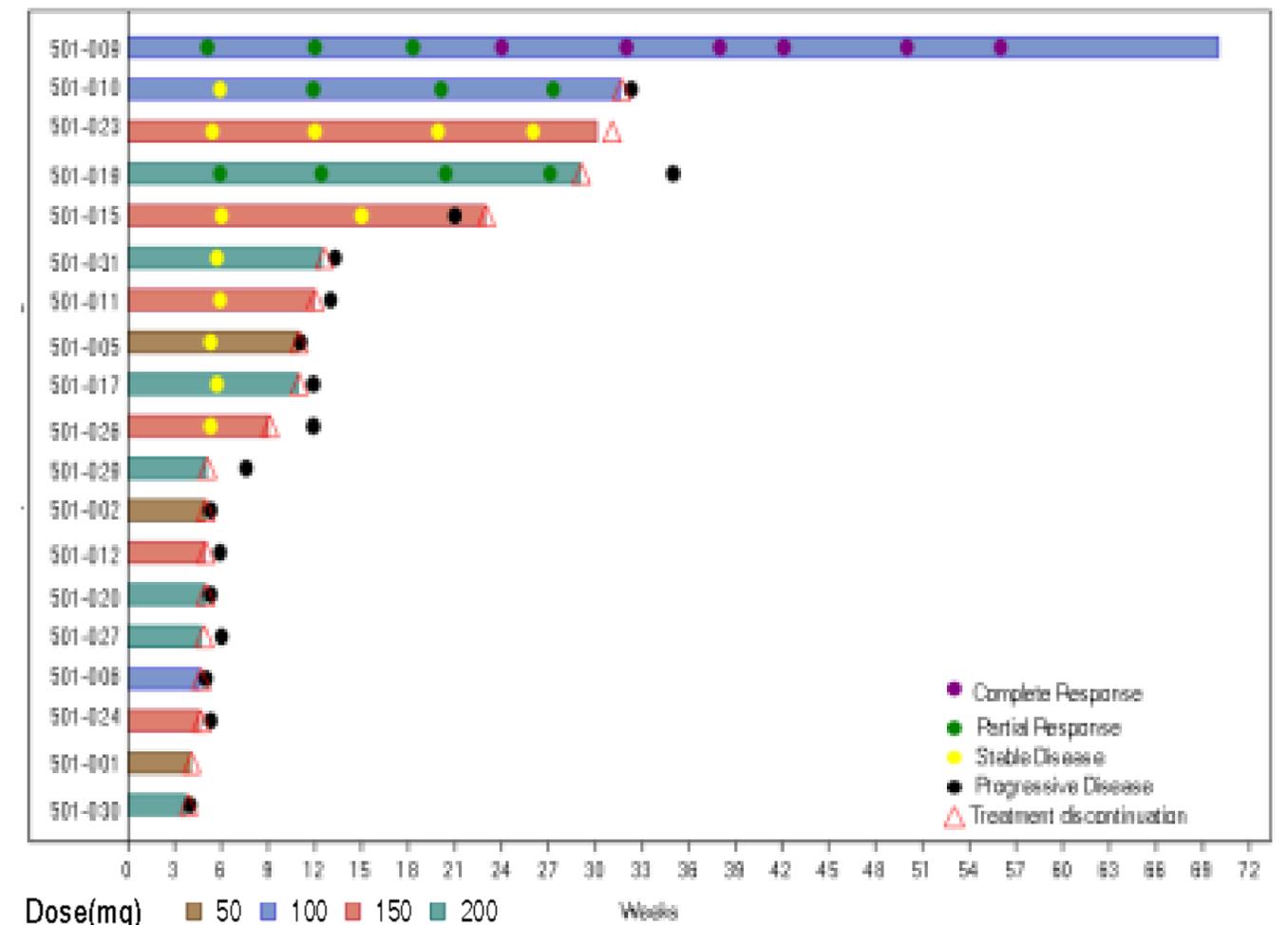
Ph Ib IO resistant/relapsed patients| combination with pembrolizumab

### Overview & Tolerance

Treatment Related AEs (at least Grade 3) by Preferred Term					
	50 mg (n=3)	100 mg (n=3)	150 mg (n=6)	200 mg (n=7)	Overall (n=19)
Any drug-related AEs with Severity Grade at least 3, n(%)	0	1 (33.3)	2 (33.3)	3 (42.9)	6 (31.6)
Platelet count decreased	0 (0.0)	0 (0.0)	2 (33.3)	2 (28.6)	4 (21.1)
Neutrophil count decreased	0 (0.0)	1 (33.3)	1 (16.7)	1 (14.3)	3 (15.8)
Adrenal insufficiency	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (5.3)
Anemia	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (5.3)
Febrile neutropenia	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (5.3)
Lymphocyte count decreased	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (5.3)
White blood cell count decreased	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (5.3)

- MTD not reached, No DLT observed
- **RP2D** is determined as **150mg QOD**
- No new tolerance finding when combined with pembrolizumab
- PK: AUC & Cmax generally increase dose proportionally over the dose range of 50-200 mg.
- PD: MIC-1(biomarker of TP53 activation) serum increase was exposure dependent within the dose range.
- Activity: **ORR: 16.7%** (1 CR|2PR) + 7SD = **DCR: 55.5%**
  - Resp: CR-Ovarian | PR-NSCLC, Appen. Adeno. | 7SD | 8PD

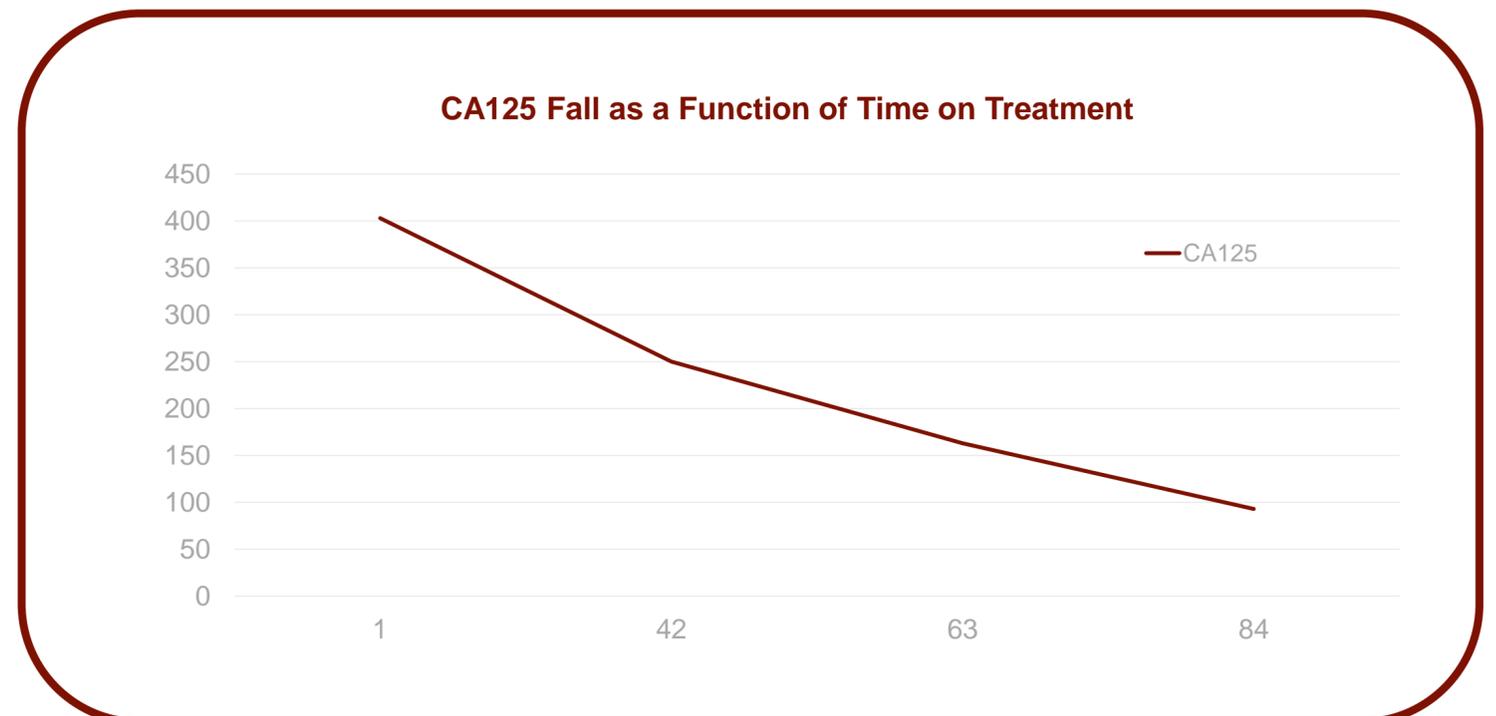
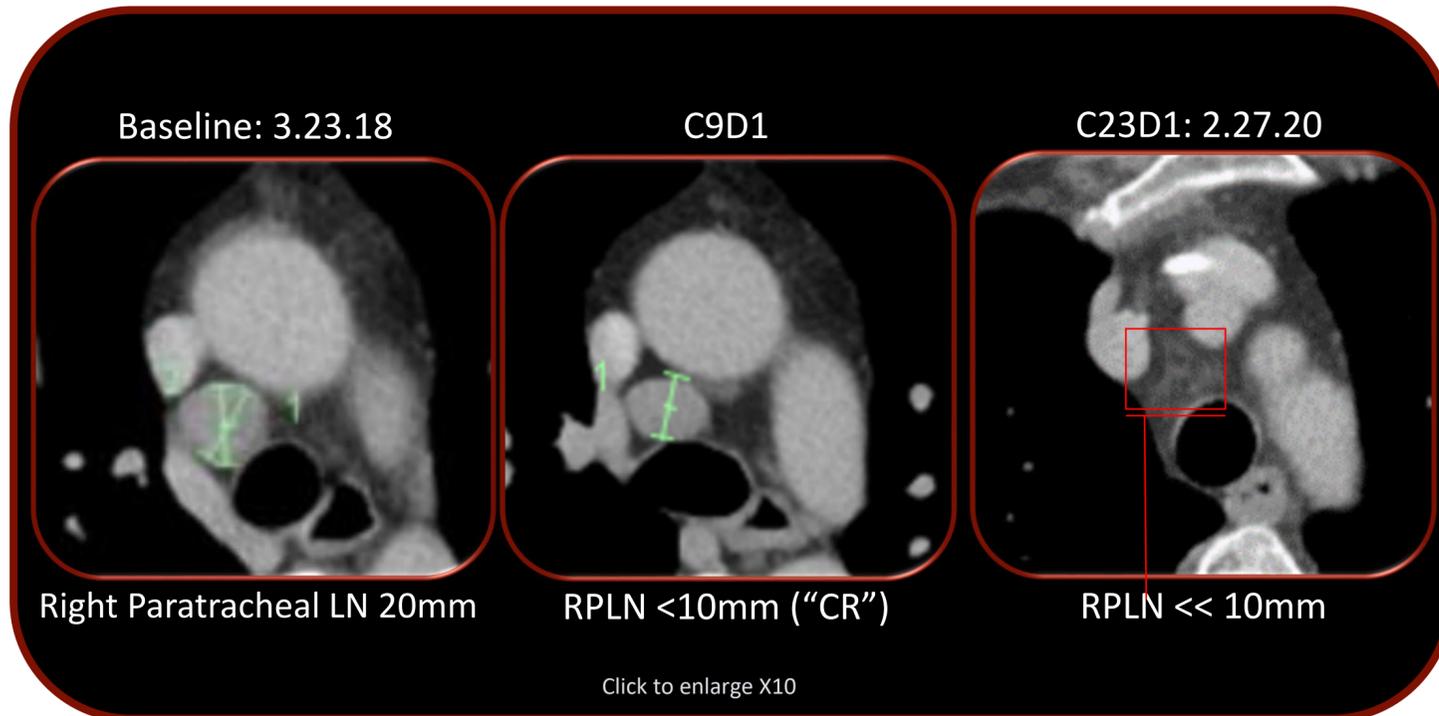
### Overview & Treatment Duration



# APG-115: Promising Activity

## Ph Ib | Combined with pembrolizumab

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



Treatment History			Clinical Trial
Initial Tx	Tx		
Neoadjuvant • Paclitaxel • Carboplatin • TAH BSO	Adjuvant • Carboplatin • Docetaxel	Relapse <math>< 6\text{mo.}</math> • <u>Doxil</u> • Topotecan • Bevacizumab • PD XMT1536	APG-115 (150mg) & Keytruda (200mg)

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

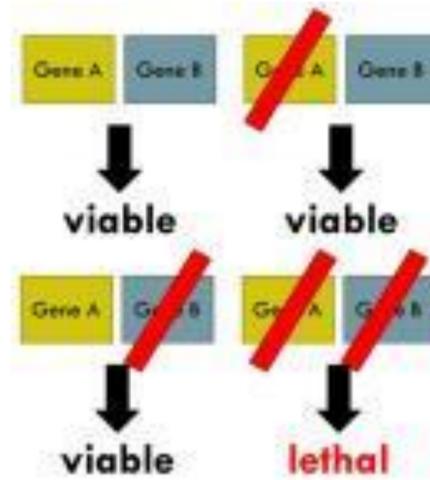
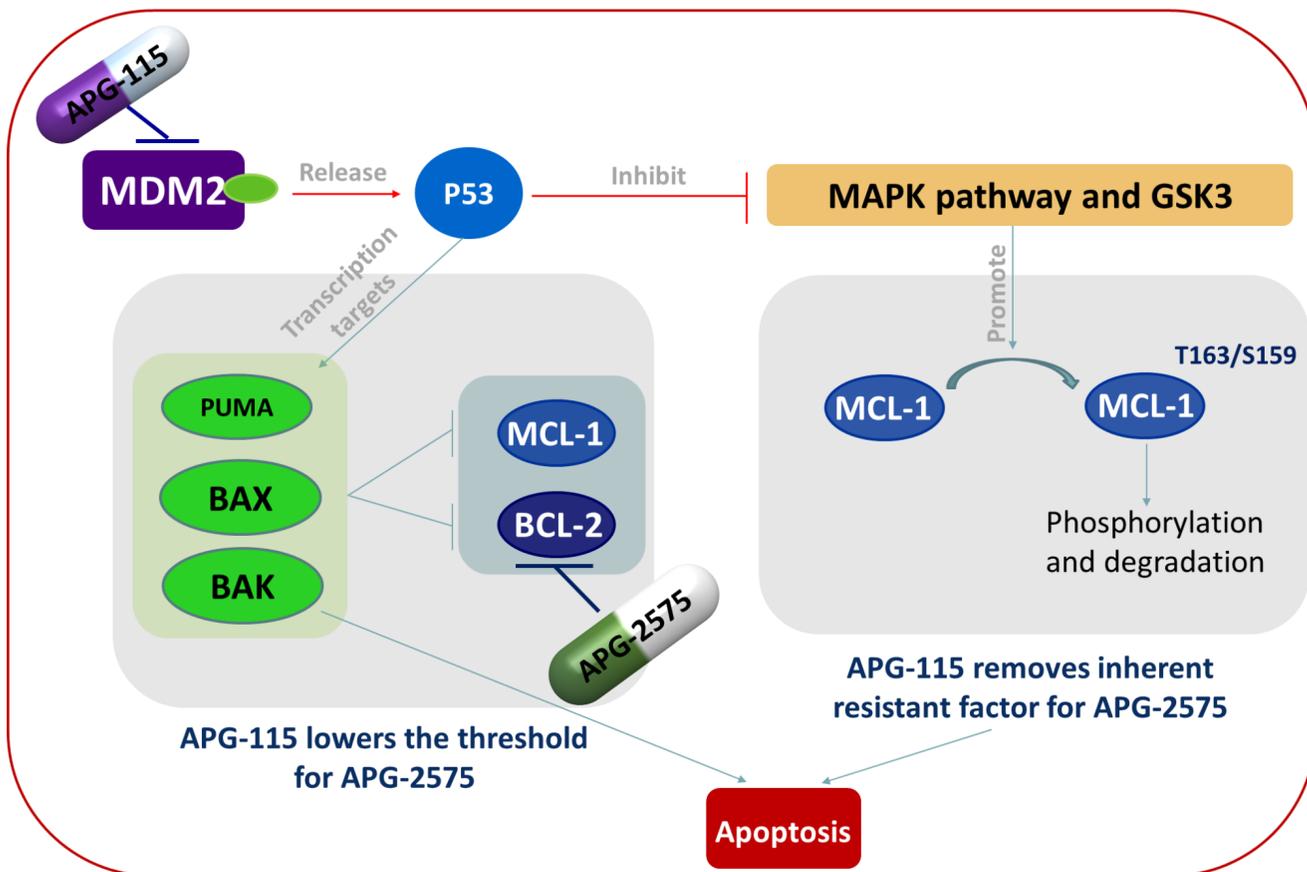
Activity(N=18) ;	Tolerance
1 CR   2PR   7SD ORR = 16.9%   DCR= 55.5%	The combination is well-tolerated No DLTs, No additive AEs

# Synthetic Lethality

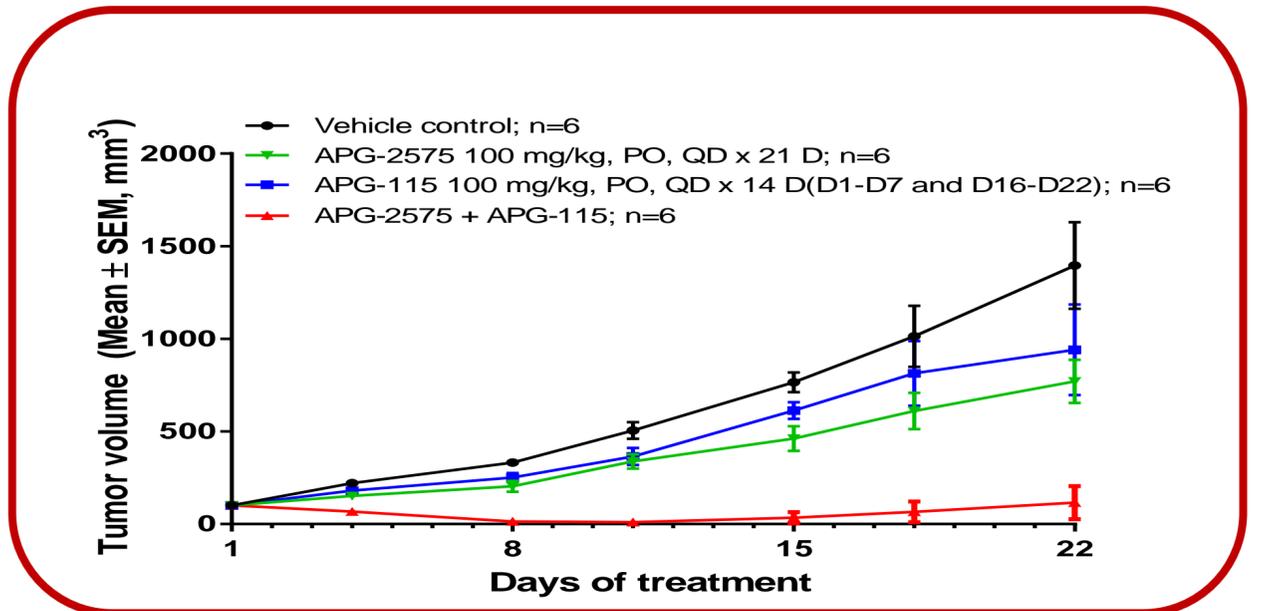
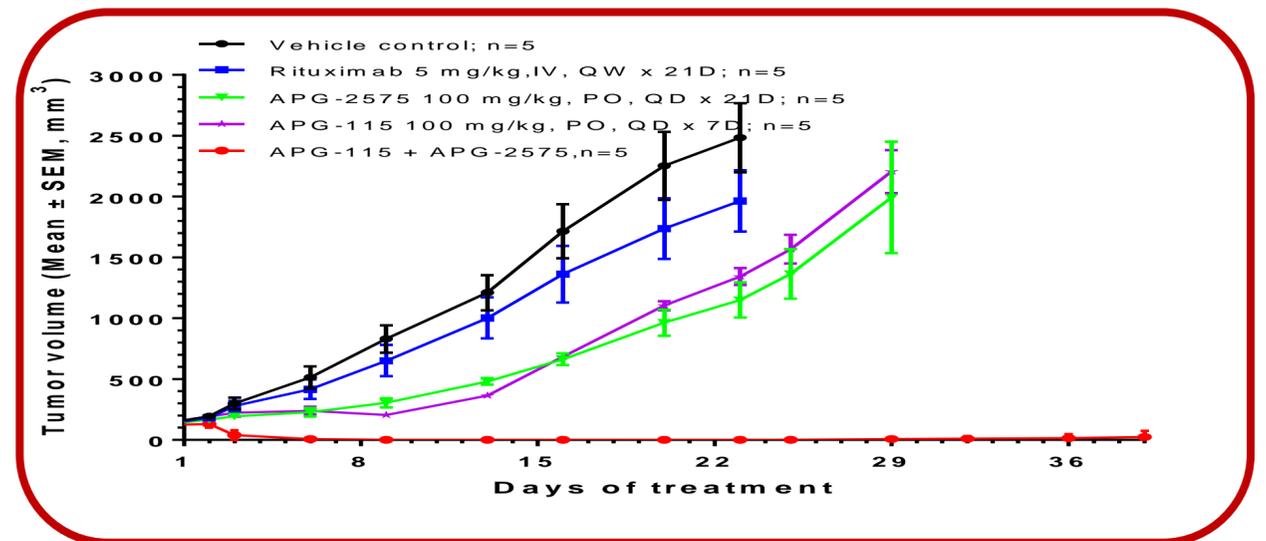
## Combination of APG-115 + APG-2575

- “Synthetic lethality” describes a strategy where blocking two mutations result in cell death, but the cancerous cells only has one mutation. By artificially inducing a second mutation the medicine can induce cancerous cell death.

### Synthetic Lethality



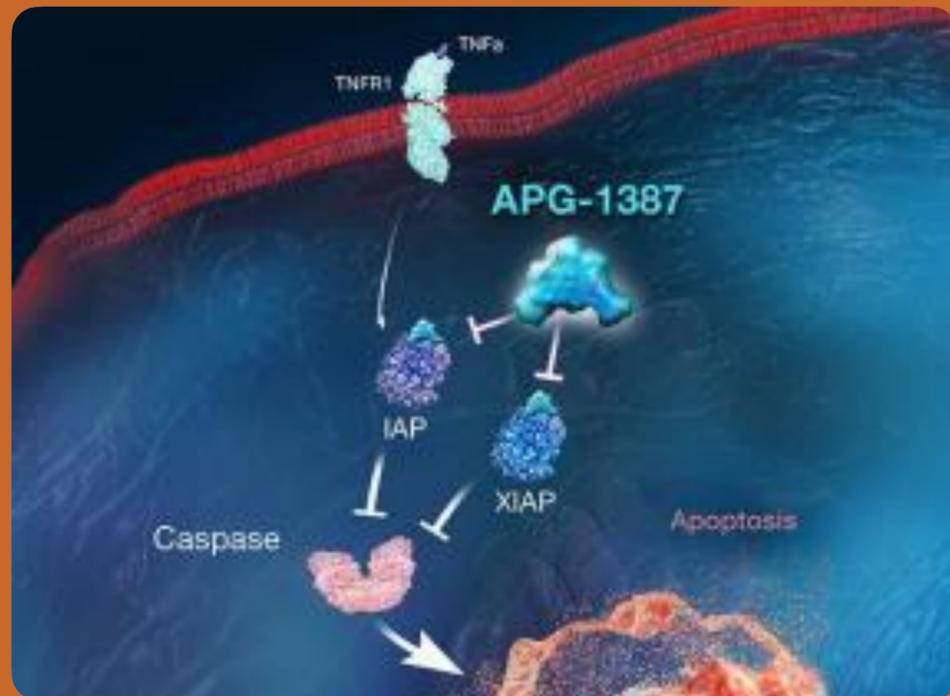
### Complete Response in Animal Tumor Models



**Use in Both Heme and Solid tumors , both oral and Chemo- Free, 1 + 1 > 2!**

# APG-1387

An Antagonist of IAP/XIAP  
(SMAC Mimetic) Dimer



## Immuno-Oncology Development

- The only IAP-targeting drug to enter clinical trials in China and completed the Phase I monotherapy clinical trials in solid tumors in US and China
- A Phase Ib clinical trial in combination with Keytruda in solid tumors ongoing
- In 2020, two Phase Ib/II clinical trials of APG-1387 combined with immunotherapy or chemotherapy in advanced solid tumors have been cleared

## CHB Developments

- A Phase Ib trial in naive Chronic Hepatitis B (CHB) patients completed the enrollment and the Phase Ib trial is ongoing
- A Phase II trial combo with NAs in CHB patients is ongoing globally

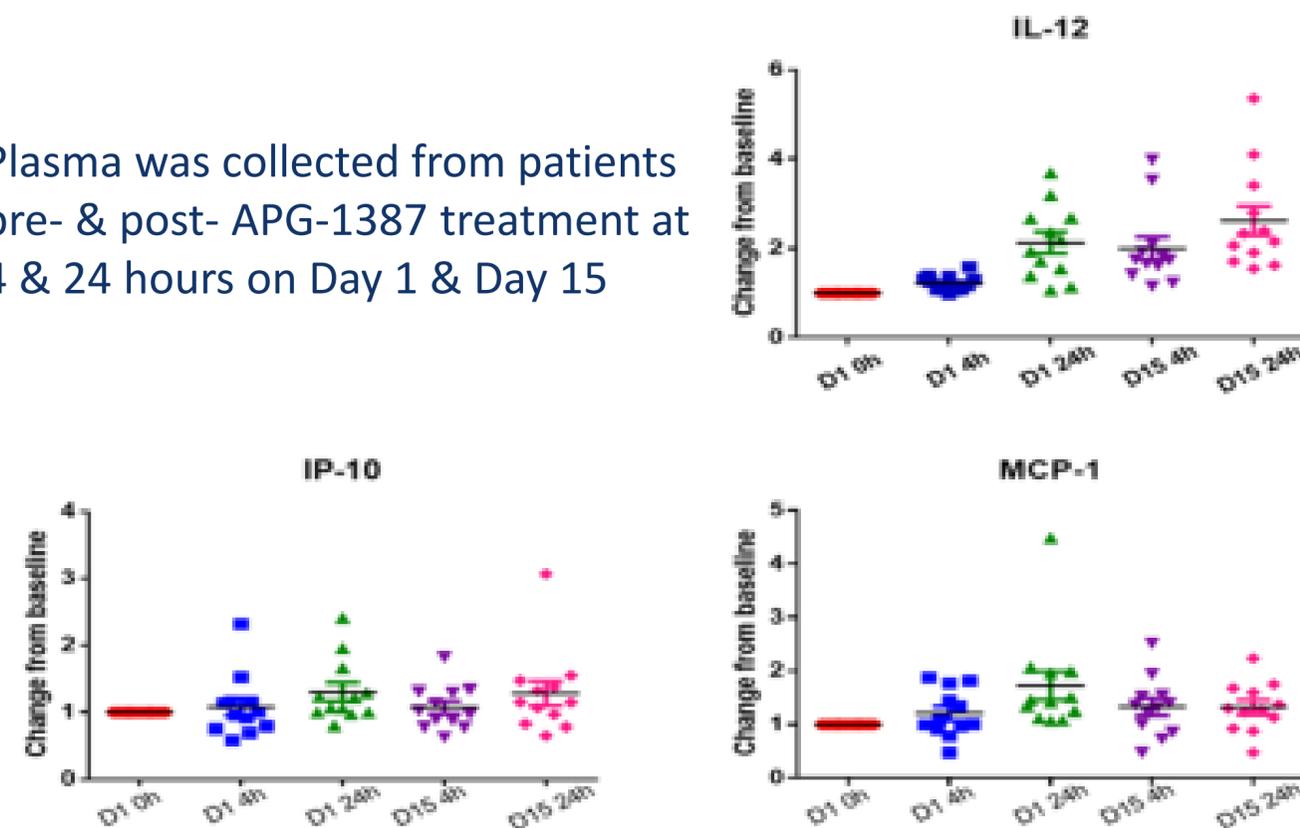
# APG-1387 Clinical Development

## Ph Ib | Immune Modulation and Activity

Ph Ib IO resistant/relapsed patients | combination with pembrolizumab

### A potential host immune modulator

Plasma was collected from patients pre- & post- APG-1387 treatment at 4 & 24 hours on Day 1 & Day 15



- Human Cytokine 30-Plex analyses showed that IL-12, IP-10, and MCP-1 were increased in the plasma 24 hours post treatment with APG-1387.
- IL-12 elevation was observed in a time- and dose-dependent manner.

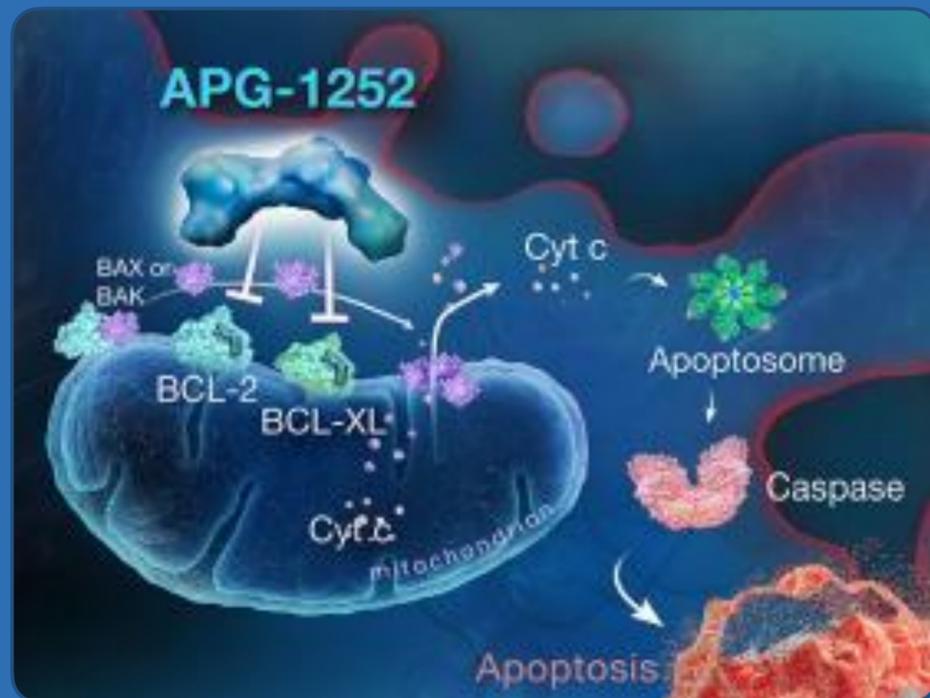
### Anti-tumor Activity

Response	All Cancers (N=41)	NSCLC (n=4)	Colorectal cancer (n=8)	Breast cancer (n=9)
ORR (CR+PR)	10.8%	50%	12.5%	11.1%
Objective responses	(4/37)	(2/4)	(1/8)	(1/9)
DCR (SD + ORR)	43.2%	100%	50%	33.3%
Disease control	(16/37)	(4/4)	(4/8)	(3/9)
Best overall response, n				
CR	0	0	0	0
PR	4	2	1	1
SD	12	2	3	2
PD	21	0	4	6
Non-evaluable	4	0	0	1

- Among 37 activity evaluable patients;
  - 4-PR (2 NSCLC | 1 CRC | 1 BC)
  - 12- SD | NSCLC cohort; 50% ORR | 100% DCR

# APG-1252 pelcitoclax

BCL-2/BCL-xL Inhibitor



## Clinical Development

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- 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

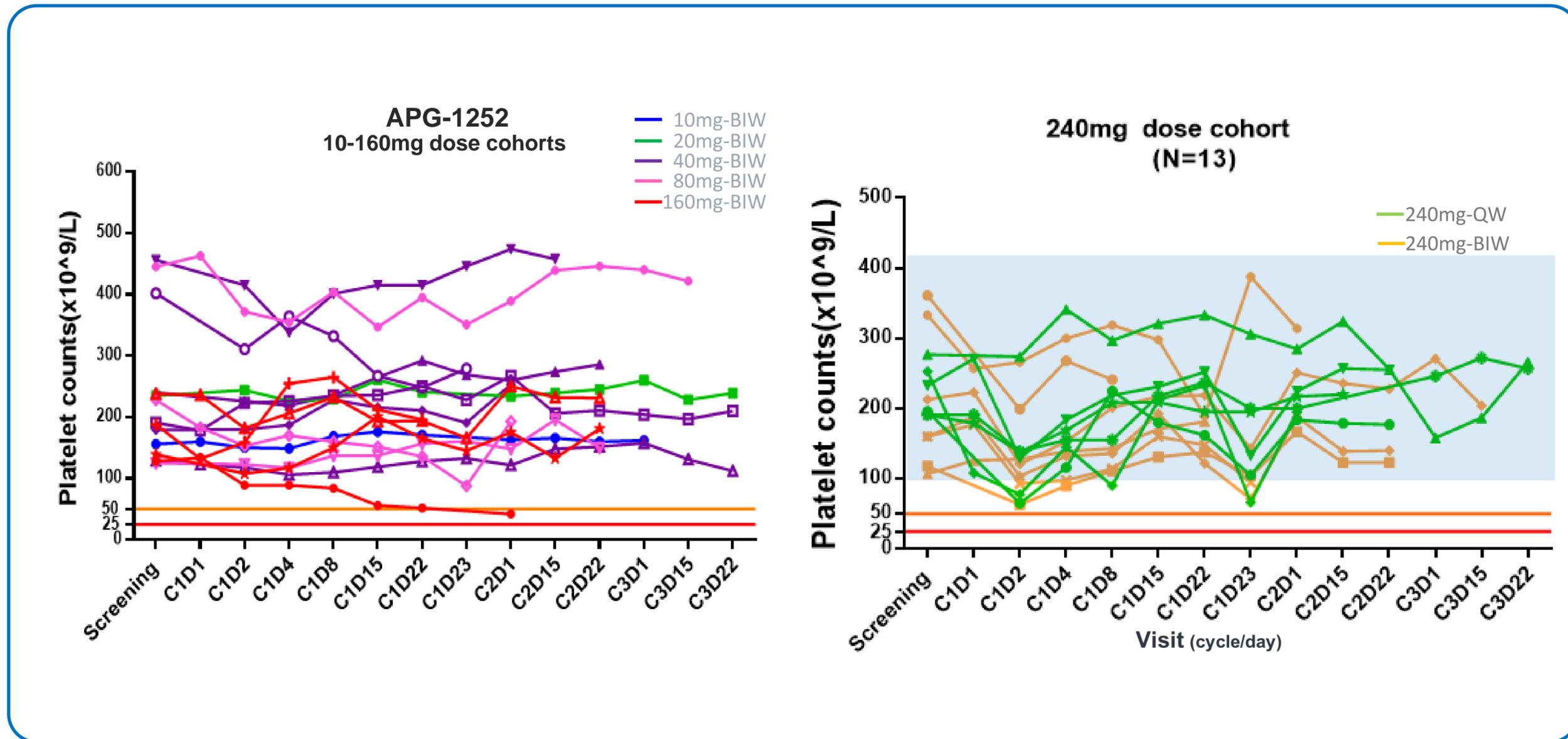
## Milestone

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- 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
- Granted ODD for the treatment of SCLC in Sep 2020

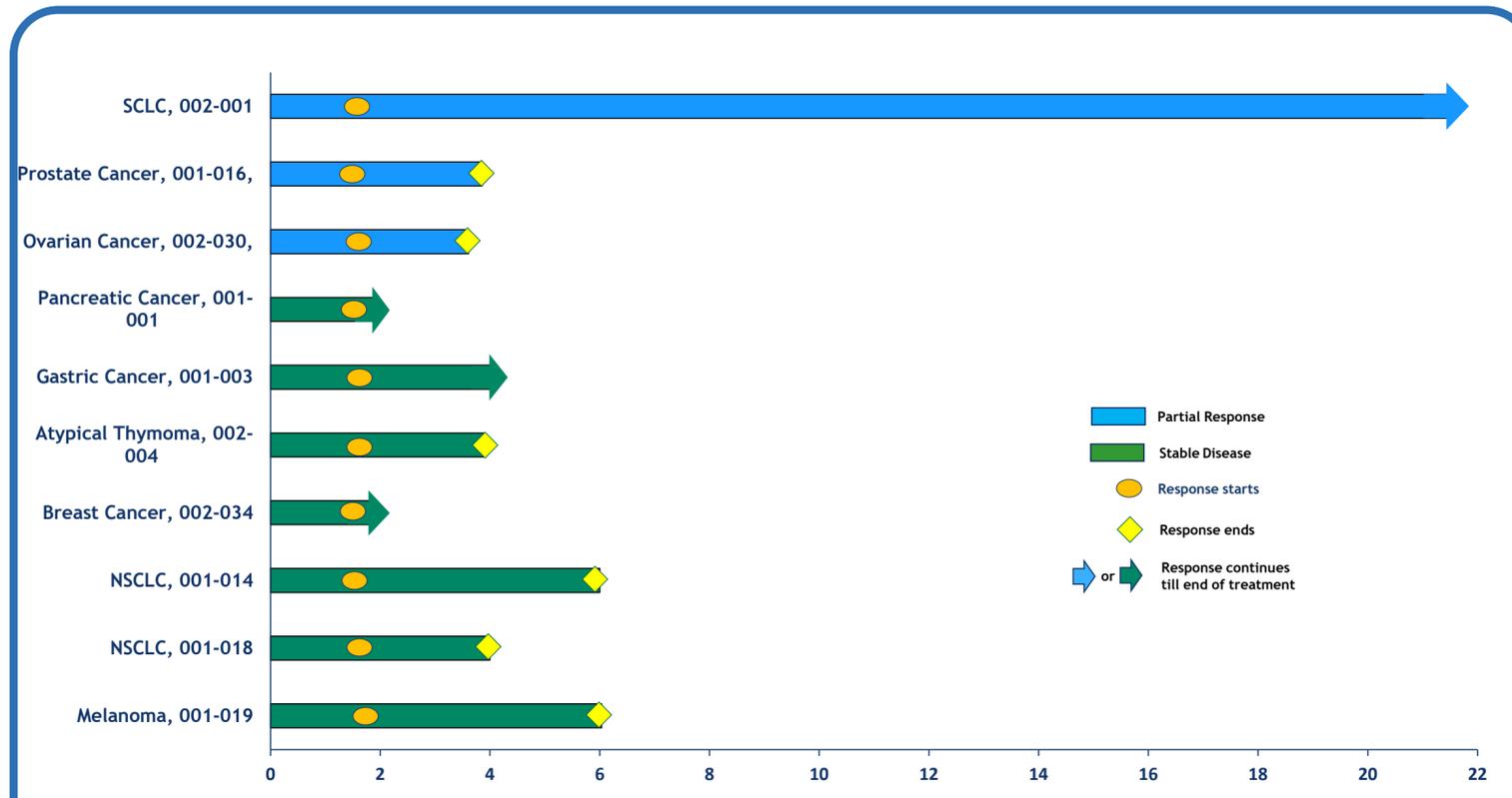
# APG-1252 Phase I Tolerance Data: Well-managed Platelet Toxicity

APG-1252 Solves Platelet Toxicity by Design; 240mg QW RP2D



# APG-1252 Phase I Interim activity Data

Single agent activity in advances solid tumors (n=42)



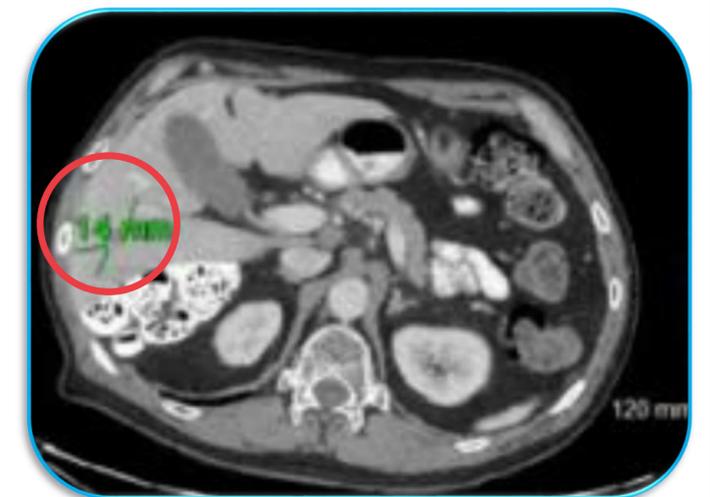
- A total of 7 patients achieved SD, 4 of them were at 10mg, BIW; 20mg, BIW , 40mg, BIW and 240mg, BIW (patient #001-001, 001-003, 002-004 and 002-034).
- Three patients achieved SD at 320mg, BIW or QW cohort.(patient #001-014, 001-018 and 001-019).
- Five patients had SD lasted for  $\geq 4$  cycles, among them 2 patients had SD lasted for  $\geq 6$  cycles.

## Durable PR in a patient with SCLC

Before APG-1252



After APG-1252



Hepatic tumor size decreases 44%  
Response maintained > 20 cycles

# Pre-Clinical Asset

EED Selective/KRAS/MDM2-p53 Degradator  
/Allosteric BCR-ABL

**Focused on validated targets with clear biomarker, clinical indications and fast regulatory approval**



**High unmet medical needs**

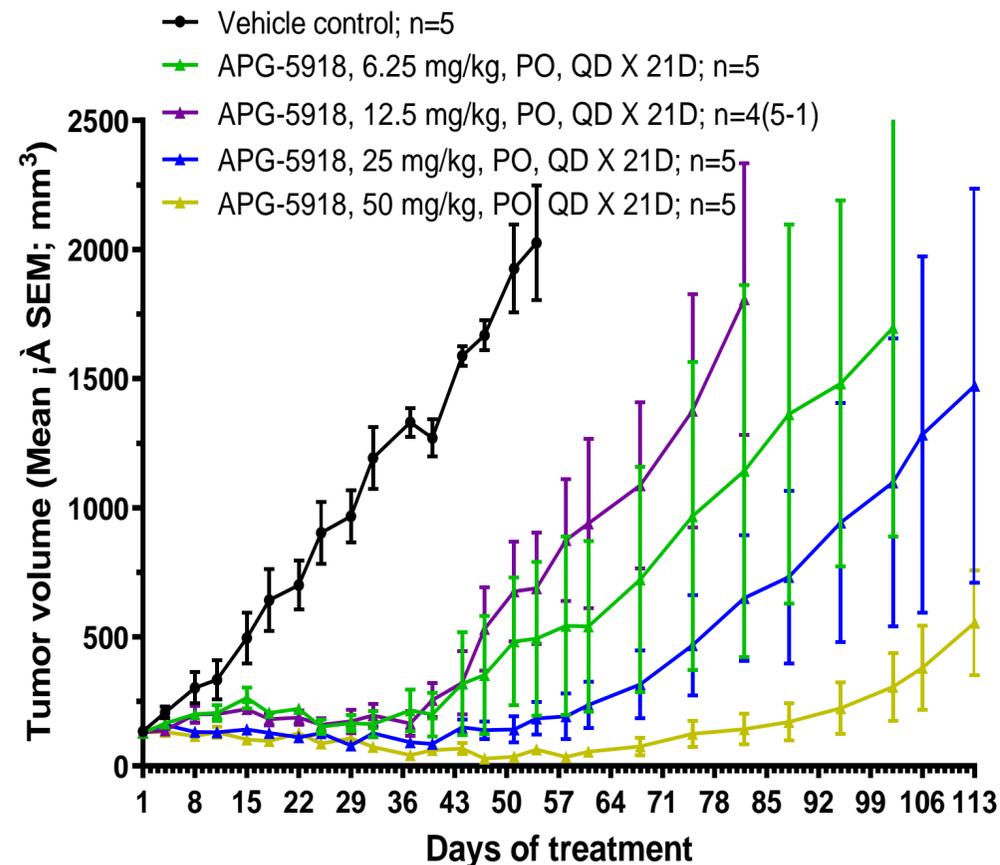
**First-in-class or best-in-class potential**

**Transformative new technology**

# APG-5918: A Best-in-Class EED Inhibitor in IND-Enabling Studies

Items		APG-5918	MAK683 (Novartis)
Binding affinity to EED protein (IC <sub>50</sub> (nM))		1.2	34 ± 18 (EED226)
Cell Growth Inhibition Assay (IC <sub>50</sub> , nM)	Karpas422	1.94±0.6	3.3
	Pfeiffer	0.14	0.7

## In vivo activity (KARPAS-422 xenograft)

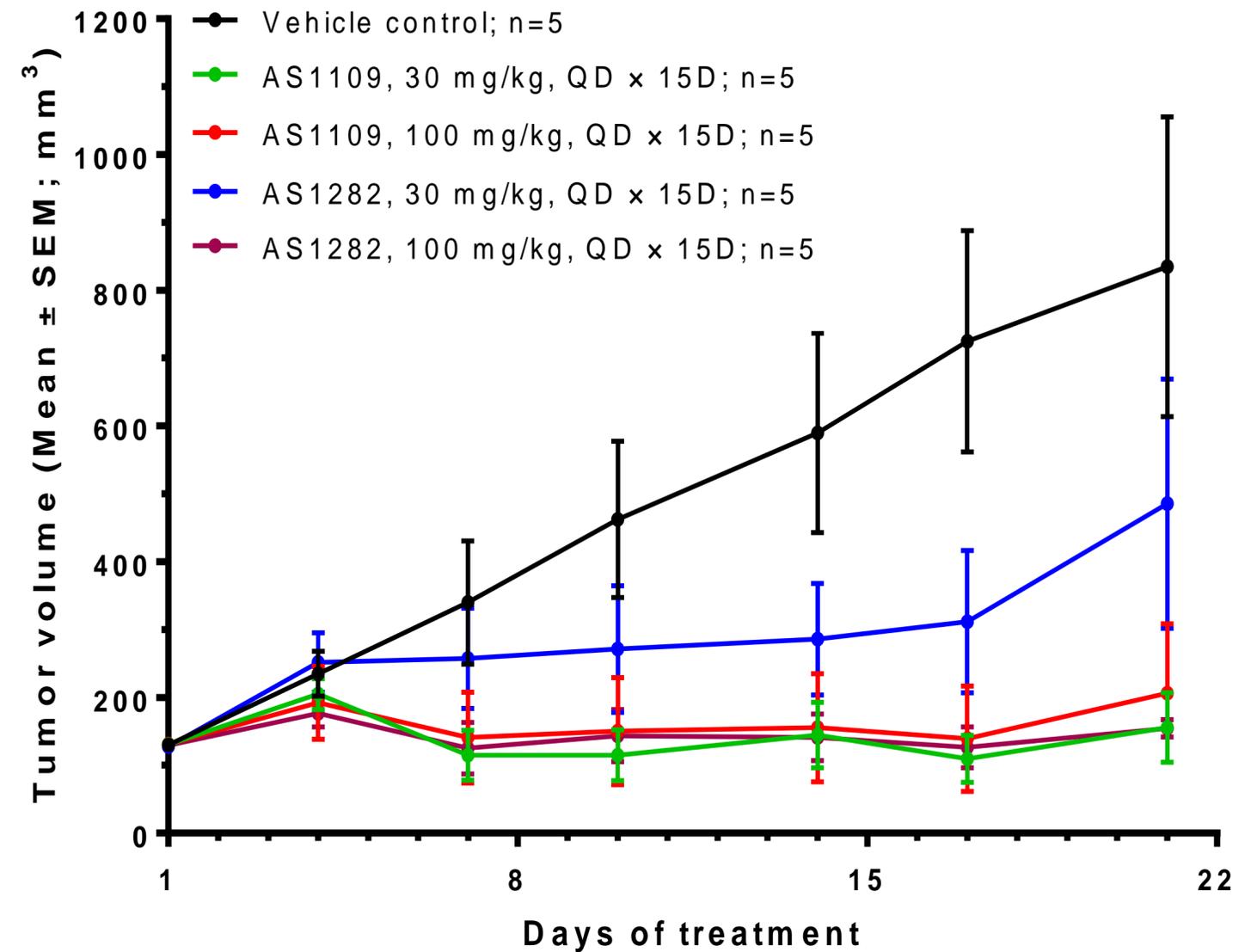


## APG-5918:

- A highly potent EED inhibitor;
- Excellent ADME and oral PK properties;
- Achieving tumor regression with oral dosing;
- Well tolerated in animals;
- Best-in-class potential;
- **In IND-enabling studies;**

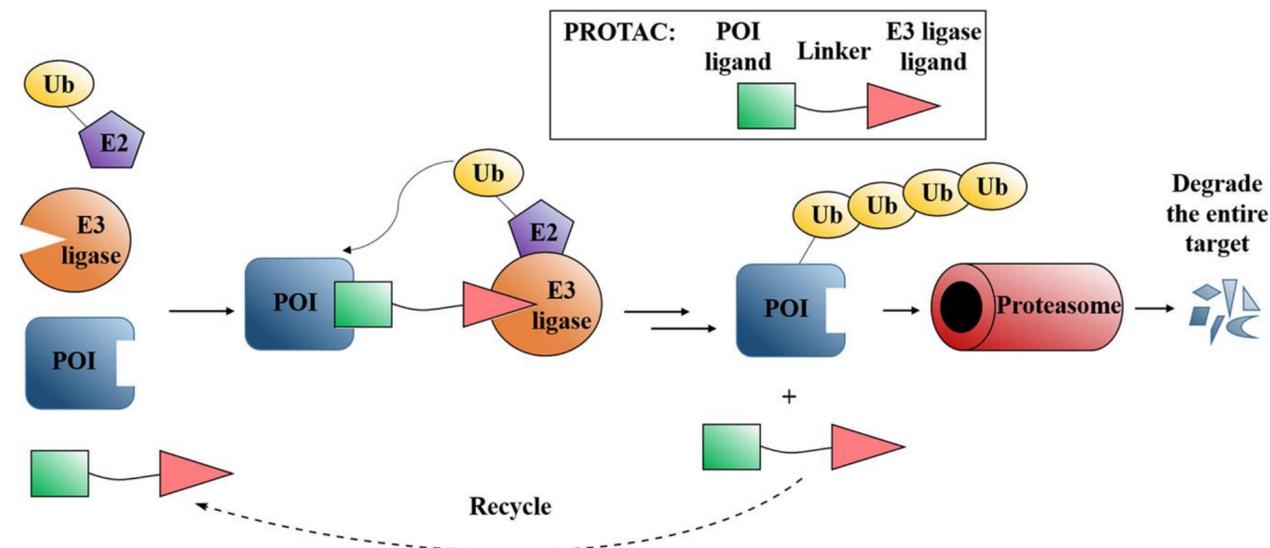
# KRAS G12C Program

- Ascentage Pharma has developed multiple classes of highly potent KRAS G12C mutant specific inhibitors;
- Lead compounds have demonstrated potent in vitro activity against cancer cells with mutated KRAS G12C, superior to AMG-510 and MRTX849;
- Lead compounds have demonstrated excellent oral pharmacokinetics, superior to AMG-510 and MRTX849;
- Lead compounds have demonstrated robust antitumor activity in animal models, superior to AMG-510;
- **Development candidate nomination on-track to be accomplished in Q1/2021**



# PROTACs: A Transformative New Therapeutic Strategy by Inducing Protein Degradation

PROTACs (proteolysis-targeting chimeras)



## ➤ PROTAC: A transformative new technology:

- Removal of a disease-causing protein by degradation instead of inhibition of the activity of a protein;
- Achieving extremely high potency and selectivity;
- Improved activity over traditional drugs (overcoming drug resistance);
- Reduced off-target toxicities;
- Dramatically expanding druggable genome;

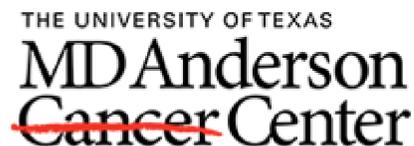


## Strategic Alliances



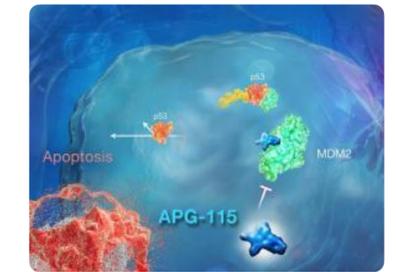
### BCL-xL

- UNITY Biotechnology ("UNITY",NASDAQ:UBX), has dosed the first patient in a Phase I clinical study of drug candidate UBX1325 in patients with diabetic macular edema (DME).
- This progress in clinical development provided Ascentage Pharma with a milestone payment according to the terms of the licensing agreement.
- Ascentage Pharma retains the rights to the compounds in the Greater China region and plans to establish a joint venture with UNITY in the future for the development and commercialization of the compound in China.



### BCL2

- Entered a global clinical collaboration with Acerta Pharma, the hematology research and development center of excellence of AstraZeneca;
- Ascentage Pharma will sponsor a clinical trial to study the combination of Ascentage Pharma's APG-2575 and Acerta Pharma's CALQUENCE® (acalabrutinib), evaluating the activity and tolerance of this combination therapy in patients with r/r CLL/SLL;
- The study has already initiated in US with the dosing of first patient, and planned to expand in Europe, and Australia.



### MDM2-p53

- Entered a global clinical collaboration with MSD;
- We will sponsor an open-label, multicenter, phase Ib/II study (NCT03611868) to evaluate the tolerance and activity of APG-115 with KEYTRUDA® (pembrolizumab) in multiple cohorts of advanced solid tumors (i, e., NSCLC, melanoma);
- The Phase II portion of the study has initiated and is expected to enroll 80 patients at multiple sites in the United States.



# Our Experienced Executives Team



**Dajun Yang, M.D., Ph.D.**  
CO-FOUNDER  
CHAIRMAN &  
CHIEF EXECUTIVE OFFICER




**Ming Guo, Ph.D.**  
CO-FOUNDER  
PRESIDENT &  
CHIEF OPERATING OFFICER




**Yifan Zhai, M.D., Ph.D.**  
CHIEF MEDICAL OFFICER




**Gang Zhu.**  
CHIEF COMMERCIAL OFFICER




**Jeff Kmetz**  
CHIEF BUSINESS OFFICER




**Thomas Knapp**  
SVP, GENERAL COUNSEL




**Su Zhang**  
CHIEF FINANCIAL OFFICER




**James (Jim) Tripp**  
SVP, PORTFOLIO MANAGEMENT  
AND HEAD OF US OPERATIONS



# Renowned & Globally Recognized Advisors



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- Professor in Medicine, University of Michigan
- Editor-in-chief, Journal of Medicinal Chemistry



Journal of  
**Medicinal Chemistry**



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- CEO of ASCO from 2006-2016
- Dean of the University of Michigan Medical School from 1998-2006
- Director of Radiation Therapy of NCI



**Jedd D. Wolchock**

M.D., PhD, FASCO

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- Director, Parker Institute for Cancer Immunotherapy at MSK
- Professor of Medicine, Weill Medical College of Cornell University



**Paul A. Bun Jr.**

M.D.

- President of ASCO, IASLC and AACI
- James Dudley Professor of Lung Cancer Research at the University of Colorado, founding director of the University of Colorado Cancer Center



**James O. Armitage**

M.D.

- Former president of ASCO
- Joe Shapiro Chair at the University of Nebraska Medical Center
- Member, Board of Directors, Tesaro



**Arul Chinnaiyan**

M.D., Ph.D.

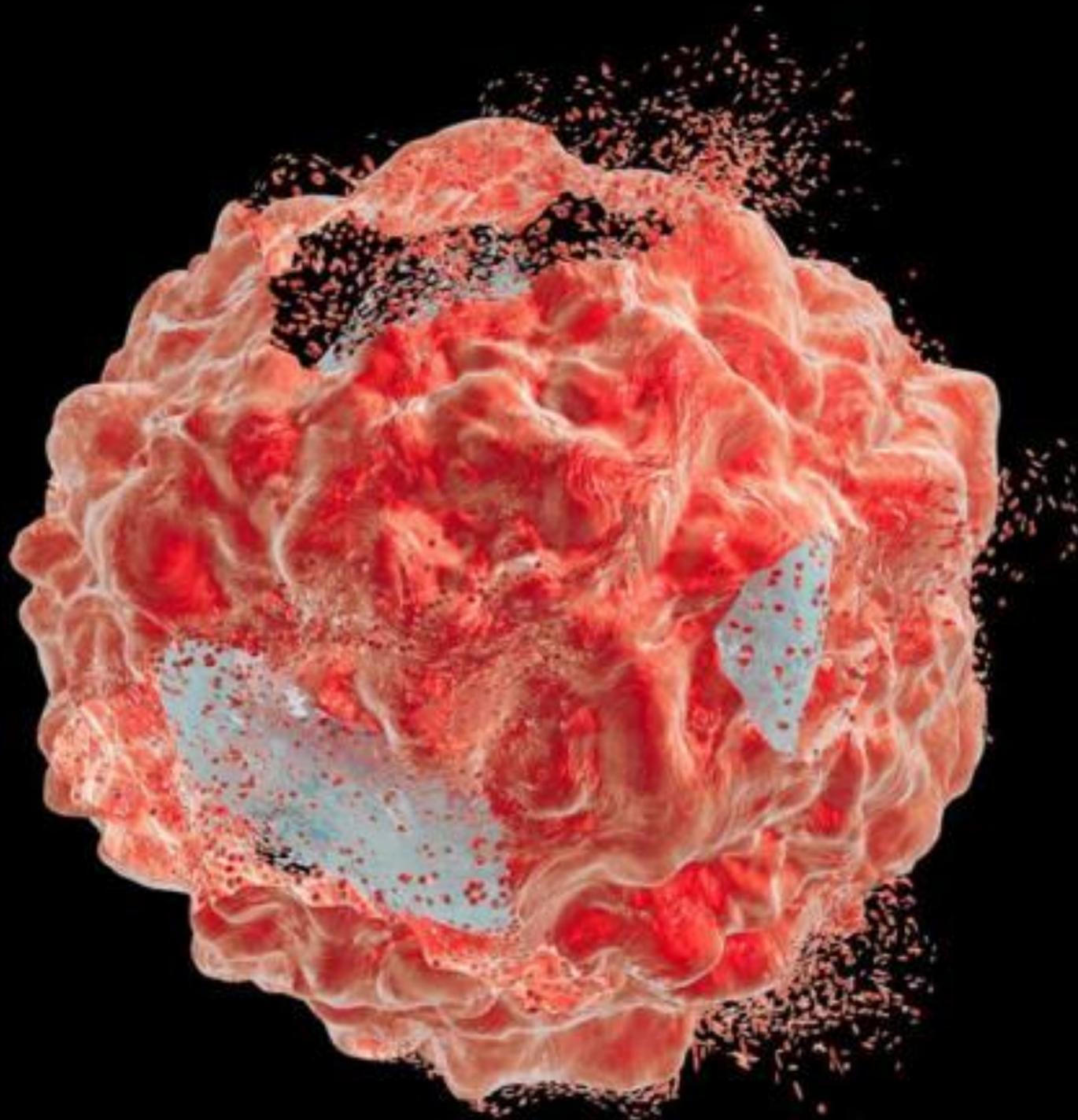
- Howard Hughes Medical Institute Investigator
- S.P. Hicks Endowed Professor at the University of Michigan Medical School



# IP Portfolio for Major Clinical Compounds

Core Compound	Patent Type	Year Patent Expires
APG-1252	Product (Core compound structure)Process; Formulation; Combination; Use	2034-2039/40*
APG-2575	Product (Core compound structure); Combination; Process; Use	2037-2039/40*
APG-115	Product (Core compound structure); Process; Combination; Use	2035-2039/40*
APG-1387	Product (Core compound structure); New indication; Combination; Use	2033-2039/40*
HQP1351	Product (Core compound structure); Process; Combination; Use; Formulation	2031-2039/40*

\*some patent types are still in the filing process



# Ascentage Pharma Group

*Advancing Therapies That  
Restore Apoptosis*