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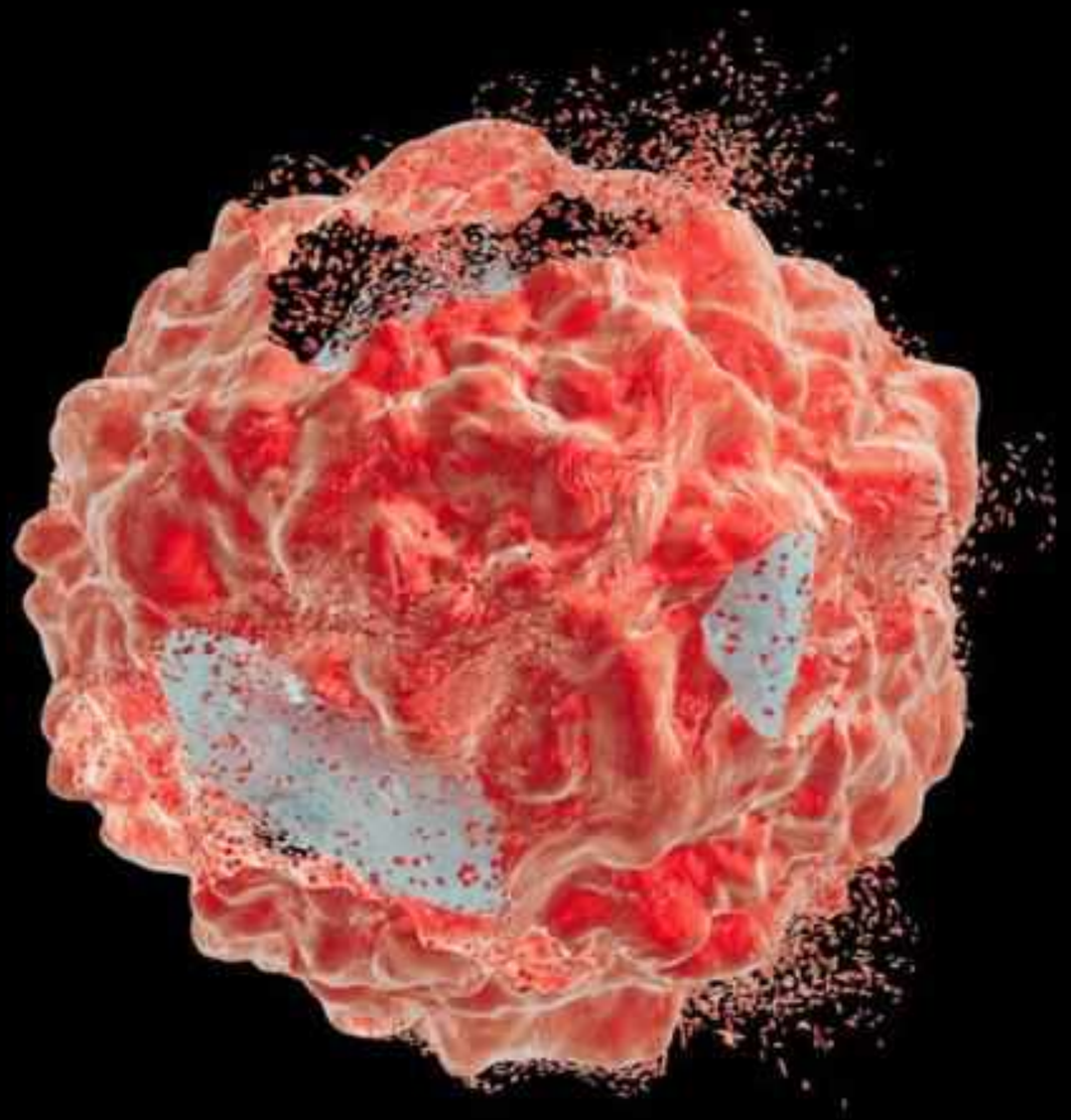
Ascentage Pharma



Ascentage Pharma Group

Advancing Therapies That Restore Apoptosis

August 2021

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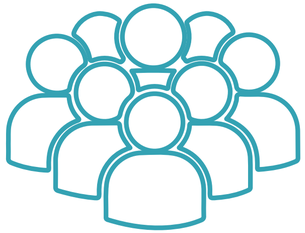
Innovative and Proprietary Platform Delivering Potentially First and/or Best-in-Class Drugs

Breakthrough science

144 issued patents

510+ pending applications

100+ publications



Strong pipeline

12 novel compounds

30+ INDS

40+ clinical trials

10+ indications

Dedicated team

1 vision: building a global biopharmaceuticals company

20+ years' commitment of executive team

500+ employees

Global development

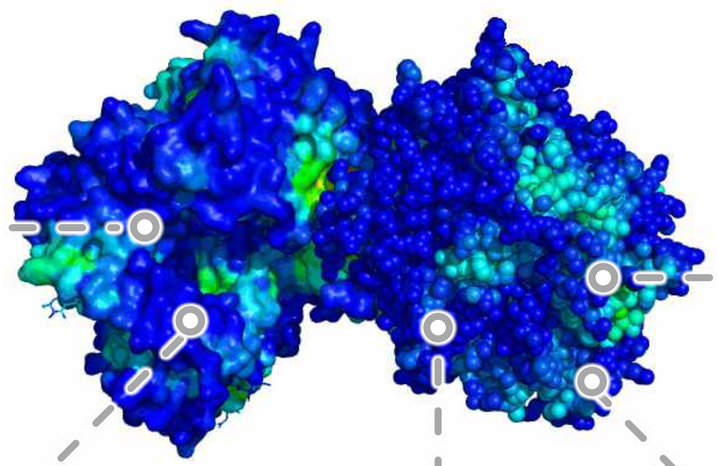
Integrated organization in **China, United States, Europe** and **Australia**

Source: Company data Note: All data as of December 31, 2020

Global Leader In 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.

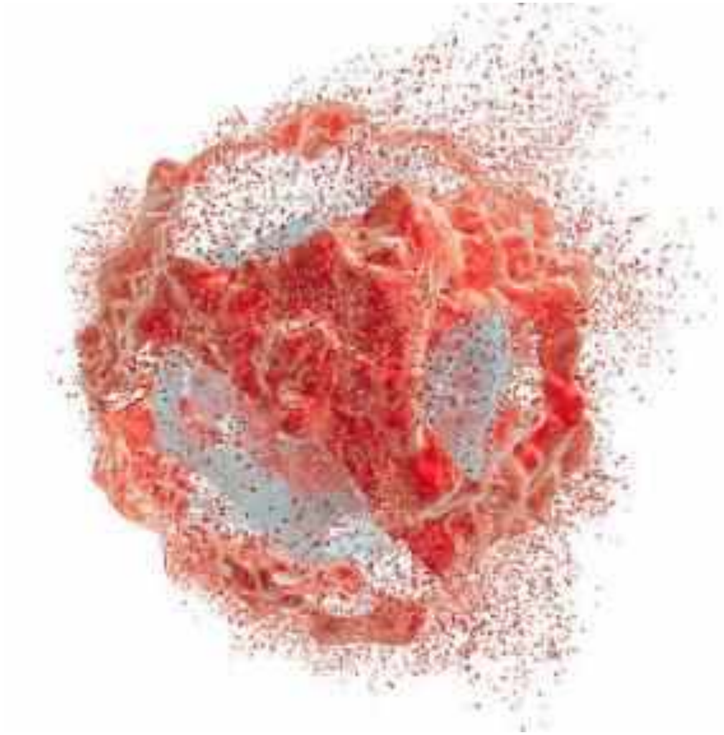
Small Molecules

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

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.

Major Achievements Over Last 12 Months



1 NDA with "Priority Review" and **"Breakthrough Therapy"** for HQP1351 (Olverembatinib) in China

Clinical Proof of Concept (POC) of APG-2575 established in r/r CLL

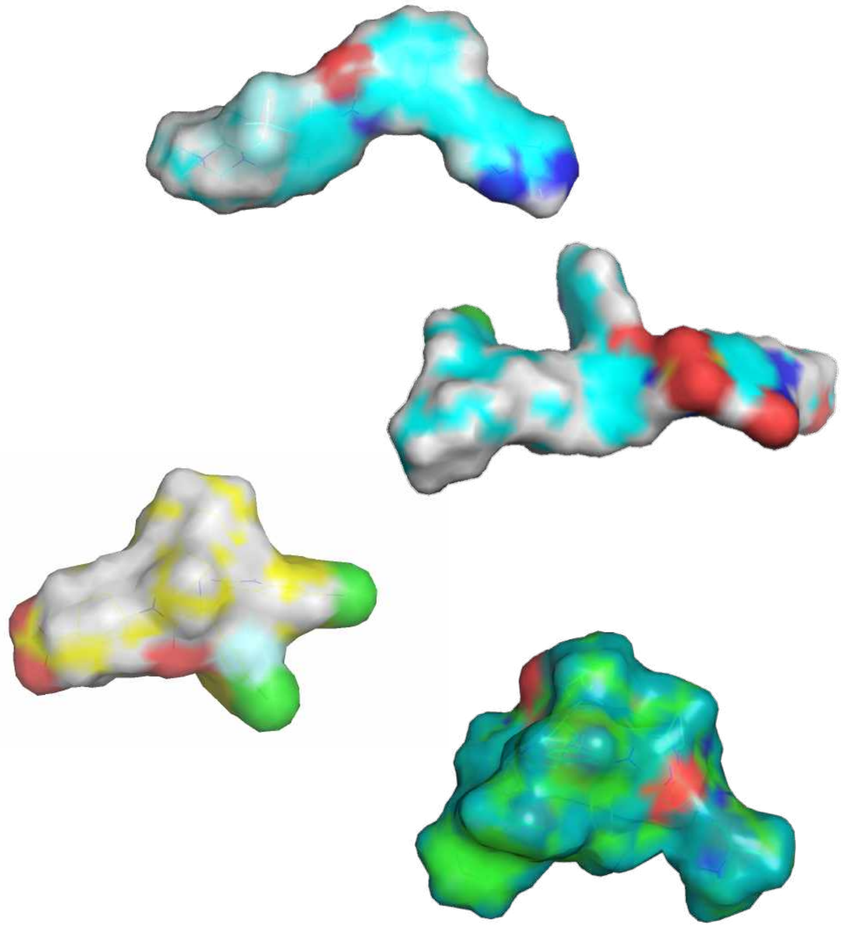
17 global studies of APG-2575 in CLL, AML, MM, etc.; entered Europe for the first time

12 ODDs and 1 FTD by US FDA

3 clinical and commercial collaborations with AstraZeneca, Merck and Innovent

12 Month Clinical Milestones

- Conditional approval and launch of **HQP1351** in China;
  NDA package submission for full approval; completion of bridging Ph Ib and initiation of discussion with FDA on pivotal study in the US
- CDE approval on the Phase II pivotal study design of **APG-2575** as a single agent for treatment of R/R CLL by the end of 2021
- **APG-115** + Keytruda® reaches POC in targeting checkpoint resistant/relapsed melanoma patients
- IAP/XIAP Dimer **APG-1387** + Keytruda® reaches Ph II POC study treating solid tumor patients
- FAK/ALK inhibitor **APG-2449** reaches POC targeting NSCLC



Source: Company data

Rich Pipeline With Significant Opportunities

Product	Target	Indications	Preclinical	Ph I	Ph II	NDA	Trial Regions	Rights regions
HQP1351	BCR-ABL/KIT	Resistant CML						
		GIST						
		Ph+ ALL						
APG-2575	Bcl-2 Selective	CLL/SLL				◆		
		WM						
		AML						
		MM						
		T-PLL						
		Solid tumors						
		ER+/HER2- Breast Cancer						
		MDS						
APG-115	MDM2-p53	Solid tumors(IO combo)				◆		
		AML,MDS						
APG-1387	IAP/XIAP	Solid tumors+IO				◆		
		PDAC+Chemo						
		HBV						
APG-1252	Bcl-2/Bcl-xL	NSCLC +TKI						
		MF						
		NET						
APG-2449	FAK/ALK/ROS1	NSCLC/ Solid tumors				◆		
APG-5918	EED Selective	Oncology/Hemoglobinopathy						
APG-265	PROTACs MDM2	Oncology						
UBX1967/1325	Bcl family	DME						

◆ POC ◆ POC in progress

Global Clinical Footprint: 40+ Studies Globally

APG-2575	CLL, MM, WM, T-PLL, AML, MDS and other hematologic malignancies; ER+ breast Ca and solid tumors
APG-115	AML, Advanced solid tumors
APG-1387	Solid tumors
HQP1351	TKI resistant CML and Ph+ ALL
APG-1252	NSCLC, MF

APG-2575	CLL/SLL

HQP1351	TKI resistant CML, GIST
APG-2575	CLL, AML, Hematologic malignancies, WM，MM, T-PLL
APG-115	AML, Sarcoma and solid tumors
APG-1387	Pancreatic, Solid tumors, HBV
APG-1252	NSCLC,NET
APG-2449	NSCLC
HQP8361	Tumors with cMET+

APG-2575	CLL, WM, AML Hematologic malignancies
APG-115	Advanced solid tumors
APG-1387	Advanced solid tumors
APG-1252	NSCLC

Source: Company data Note: All data as of December 31, 2020

More ODDs Than Any Other Chinese Biotech Companies

4 Breakthrough

- BeiGene — Zanubrutinib, 1 BTD
- 君实生物 TopAlliance — JS001, 1 BTD
- 基石药业 CStone Pharmaceuticals — Sugemalimab, 1 BTD
- 荣昌制药 RONGSCHANG — RC48-ADC, 1 BTD

40 Orphan Drug

- 亚盛醫藥 Ascentage Pharma — APG-115, APG-1252, APG-2575, HQP1351, **12 ODDs**
- BeiGene — Zanubrutinib, Tislelizumab, 4 ODDs
- 君实生物 TopAlliance — JS001, 3 ODDs
- 依生生物 YISHENG BIOPHARMA — YS-ON-001, 3 ODDs
- CARSGEN THERAPEUTICS, XWPharma, Gan & Lee, REGIMMUNE, I-MAB, Jacobio, 康宁杰瑞, HIGHTIDE, INNOCARE, 基石药业 CStone Pharmaceuticals, CHI-MED

15 Fast Track

- 亚盛醫藥 Ascentage Pharma — HQP1351, 1 FTD
- XYNOMIC Pharma — Abexinostat, 2 FTDs
- CHI-MED — Fruquintinib Surufatinib, 2 FTDs
- HIGHTIDE — HTD1801, 2 FTDs
- KBP BIOSCIENCES, 泽生科技, Akesobio, Adlai Nortye 阿诺医药, 荣昌制药 RONGSCHANG

Commercialization update

Joint Commercial team of Ascentage & Innovent will accelerate the launch of Olverembatinib

- Leveraging Innovent strong commercial team, Olverembatinib will quickly penetrate 80% of potential market before NRDL, reach higher peak sales and maximize the life cycle value.
- Sharing Innovent's commercial recourses and experience will boost the commercial capability of Ascentage.
- Ours joint commercial team is on track to optimize brand strategy, pricing strategy and NRDL negotiation strategy for Olverembatinib.

	Ascentage Solo Team		Ascentage & Innovent Joint Team	
HQP1351 before NRDL	60% CML MKT Potential	350 Hospitals	80% CML MKT Potential	800+ Hospitals
HQP1351 after NRDL & prepare for APG-2575	80+% CML MKT Potential	800+ Hospitals	90+% CML MKT Potential	2000+ Hospitals

Landmark Strategic Collaboration With Innovent

Landmark multi-part deal in China of **up to USD 245m** between two leading Chinese biopharma companies

Strategic equity investment signifying Innovent's **strong recognition** of our R&D capabilities and our growth potential

To jointly develop HQP1351 and APG-2575 in China: **de-risking, cost sharing** and **keeping the upside**

Two promising combination therapies of APG-2575/HALPRYZA (CD-20) and APG-2575/letaplimab (CD-47) with **synergy** in various oncology indications

Combined sales force of 2,100+ to support the commercialization of HQP1351

To bring in **USD90m cash** near term to support clinical development of our pipeline

Multiple Ongoing Strategic Alliances

BCL-xL

UNITY BIOTECHNOLOGY

- 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

BCL-2

AstraZeneca

- Entered a global clinical collaboration with Acerta Pharma, the hematology research and development center of excellence of AstraZeneca
- A clinical trial of Ascentage Pharma's APG-2575 combined with Acerta Pharma's CALQUENCE® (acalabrutinib), evaluating the efficacy and safety of this combination therapy in patients with r/r CLL/SLL is on going

MDM2-p53

MSD

- Entered a global clinical collaboration with MSD
- An open-label, multicenter, phase Ib/II study (NCT03611868) , evaluating the safety and efficacy of APG-115 with KEYTRUDA® (pembrolizumab) in multiple cohorts of advanced solid tumors (i, e., NSCLC, melanoma) is ongoing

BCR-ABL & BCL-2

Innovent

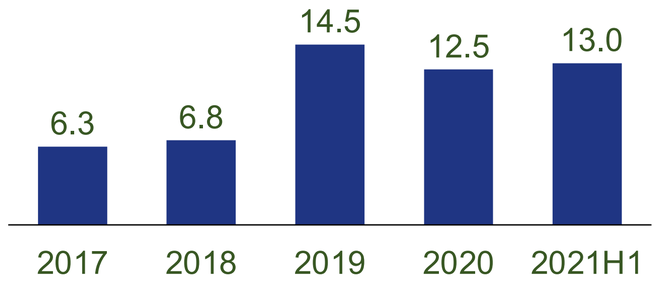
- Ascentage agreed to grant to Innovent the right to develop HQP1351 in China and to commercialize HQP1351 in the cities within China being allocated to Innovent.
- Two companies jointly develop and conduct clinical trials of the combination therapy involving APG-2575, in combination with the CD20 Antibody and the CD47 Antibody for the treatment of certain indications.
- Innovent agreed to US$50 million worth of Ascentage Pharma's common stock. Ascentage Pharma will grant Innovent stock warrants that will allow it to acquire additional Ascentage Pharma's common shares for a total consideration of US$50 million

UNIVERSITY OF MICHIGAN · MAYO CLINIC · THE UNIVERSITY OF TEXAS MD Anderson Cancer Center · Dana-Farber Cancer Institute · TopAlliance Biosciences · NIH NATIONAL CANCER INSTITUTE

Key Financial Highlights

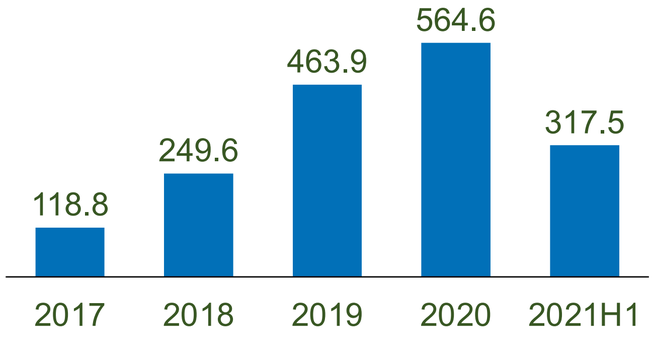
Revenue[1]

(RMB mm)



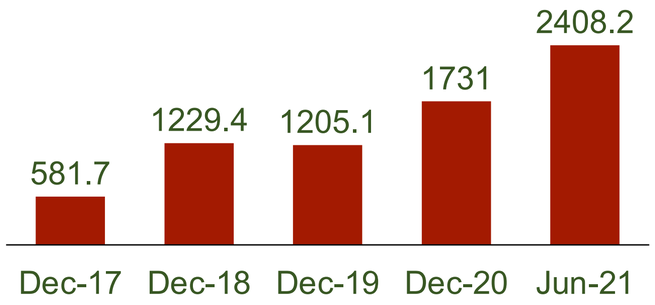
R&D Expense

(RMB mm)



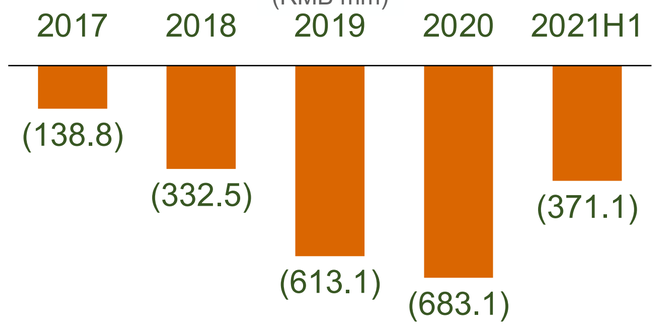
Total Assets

(RMB mm)



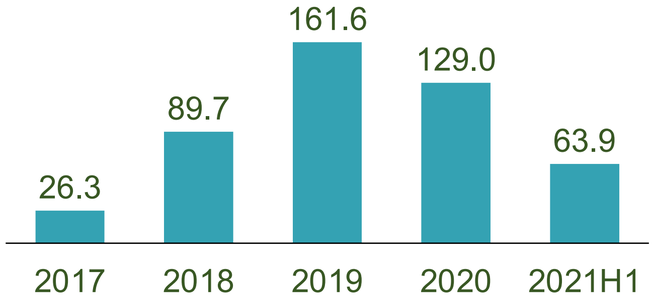
EBIT[2]

(RMB mm)



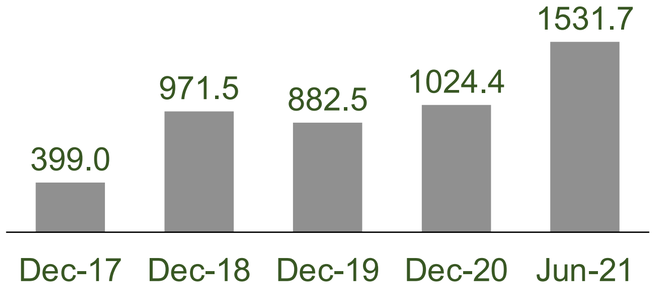
OPEX

(RMB mm)



Cash & Equivalents[3]

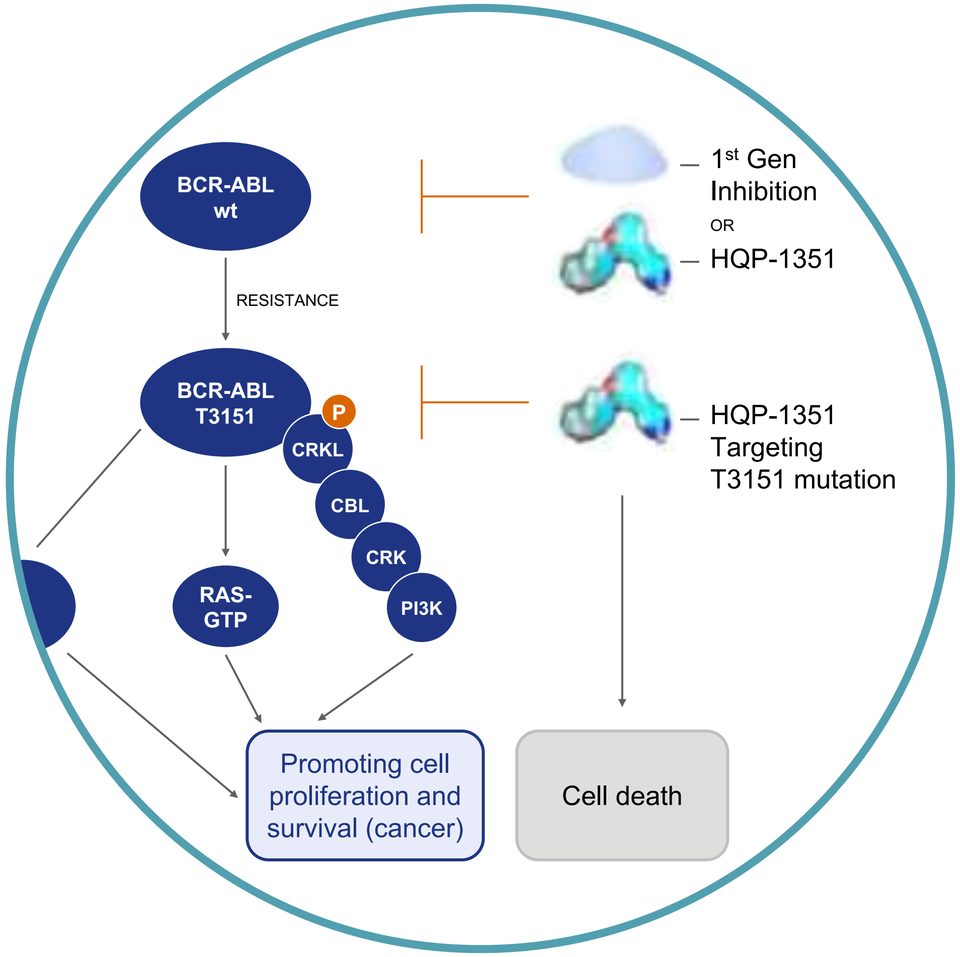
(RMB mm)



1）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 products

HQP1351
Olverembatinib Overview

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



Huge Unmet Medical Needs in CML

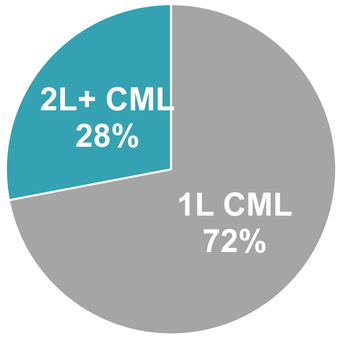
CML Patient Numbers

51,000+
CML patients in US

75,000+
CML patients in China

CML	$5.5b Market	33.3K Incidence	135K Prevalence

China's CML patients by lines of treatment



Though TKIs have revolutionized management of CML, many patients develop resistance or intolerance to available TKIs

1st gen TKI
Imatinib

Fails in up to 40% of patients due to BCR-ABL1 resistant mutations, intolerance, and/or suboptimal adherence to therapy schedule.

2nd gen TKIs
Dasatinib and Nilotinib

Treatment failure with 2nd gen TKIs portends a poor prognosis among the estimated 37–52% of patients[1]

The only 3rd gen TKI
Ponatinib

Until now, only Ponatinib has been able to overcome TKI-resistance, including T315i mutation

The only approved 3rd gen TKI Ponatinib received Black Box Warnings due to cardiovascular events.

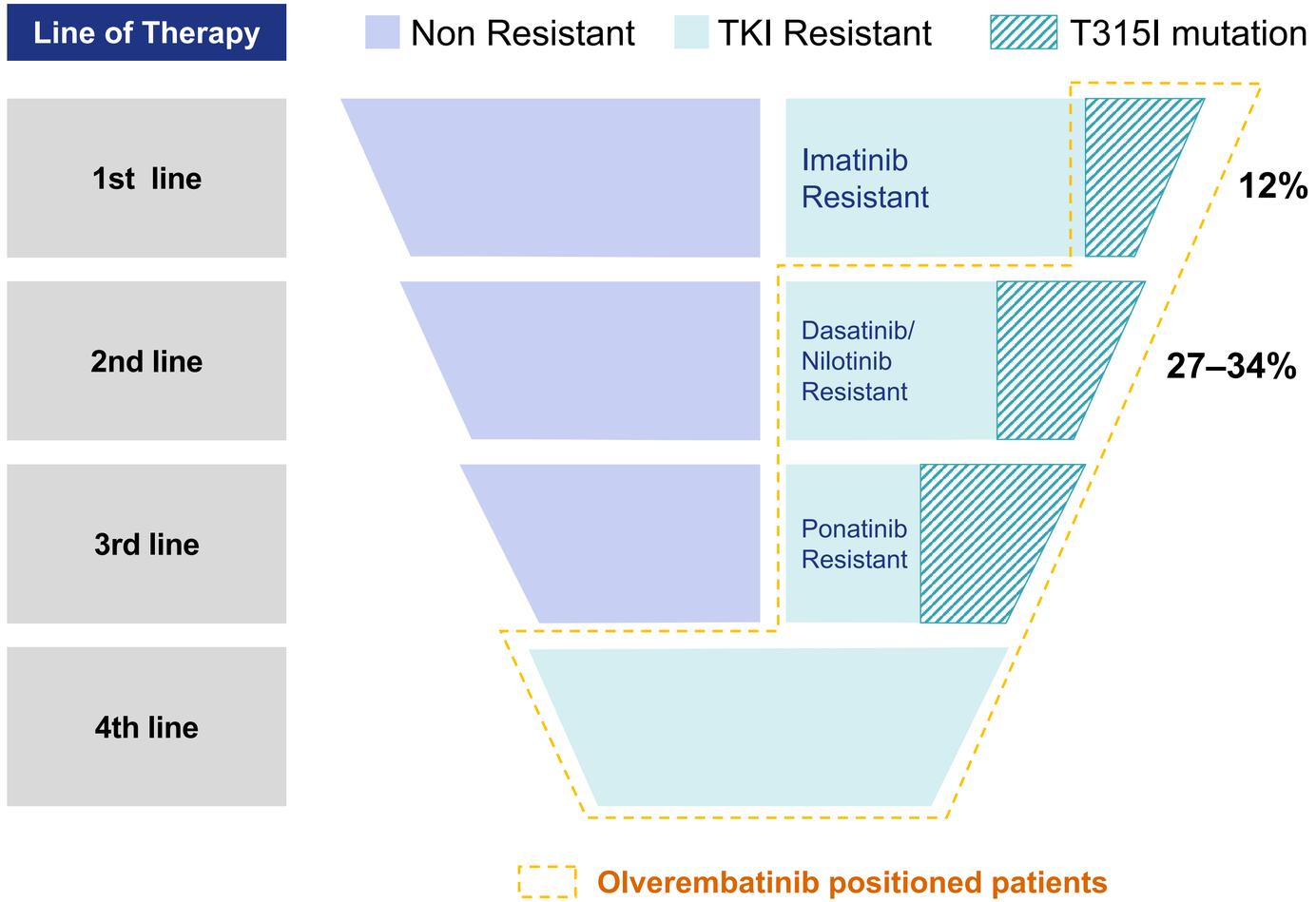
None of the above TKIs are effective in the presence of some "compound" mutations.

HQP1351: **First** 3rd generation BCR-ABL TKI developed in China, **Second** entering NDA globally

1. Ren X et al. J Med Chem 2013;56:879-894.

China CML TKI-Resistance Patient Pool

CML patients treated with TKI



For illustrative purposes of patient size

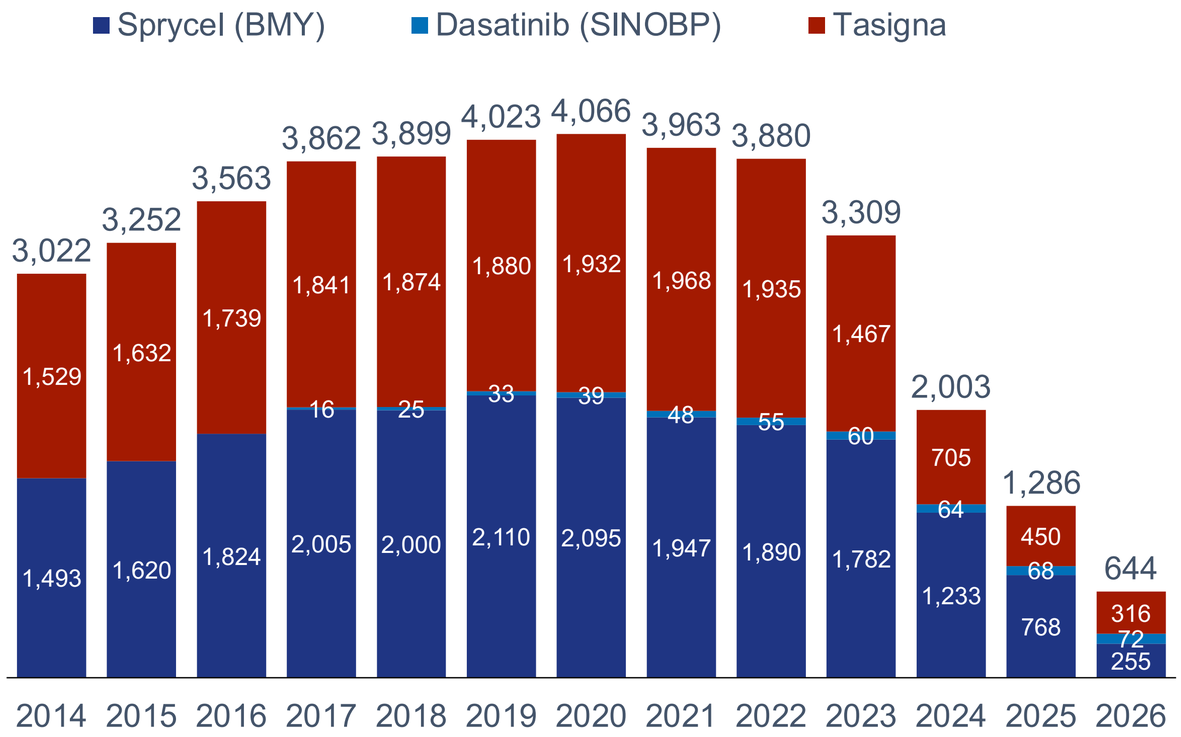
TKI resistance & T315I mut share

- In a Chinese review analysis, 52.7%, 21.8%, 25.5% cases among TKI resistant CML patients experienced resistance to imatinib , nilotinib and dasatinib[1]
- Over **half** of imatinib-, nilotinib-, and dasatinib-resistant cases developed BCR-ABL mutation1
- **T315I mutation** was the most frequent mutation detected in imatinib-, nilotinib-, and dasatinib-resistant cases, accounting for 12.3%, 27.3%, and 34.1%[1]

Source:1. Chin J Hematol, 2020,41(06): 469-476

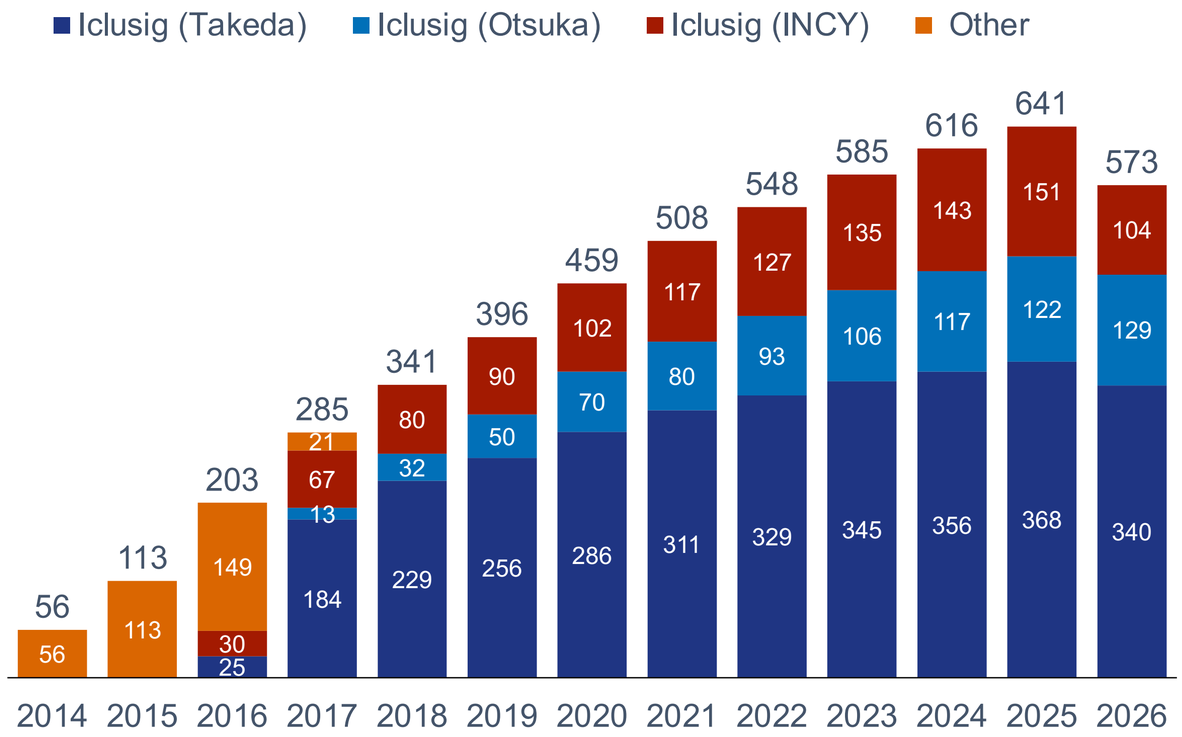
Large Potential Market for 3rd Gen BCR-ABL Inhibitors

Worldwide Sales (US$M)



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

Worldwide Sales (US$M)



Global sales of ponatinib forecasted at $641M in 2025

Source: Global Data, Drug Sales and Consensus Forecast View, Extracted Date: 27-Jan-2020， Evaluate Ltd

Development Milestone: From IND Approval to NDA in 4 Years

2015

- In Apr, submitted an IND TKI resistant CML in China

2016

- In Feb. NMPA issued a “one-time umbrella approval” for r/r CML

2018

- In Jul, held a pivotal Phase II clinical trial kick-off meeting with PI

2019

- In Jan, awarded “National Major Innovative Drug Project”
- In Jul, entered Phase Ib clinical study for TKI rCML in US
- In Sep, finished enrollment of 2 pivotal Phase II trials in China
- Results of Ph I trial of HQP1351 in CP|AP TKI resistant / intolerant CML **were orally presented at ASH 2018, 2019 and 2020**, nominated as “Best of ASH” in 2019

2020

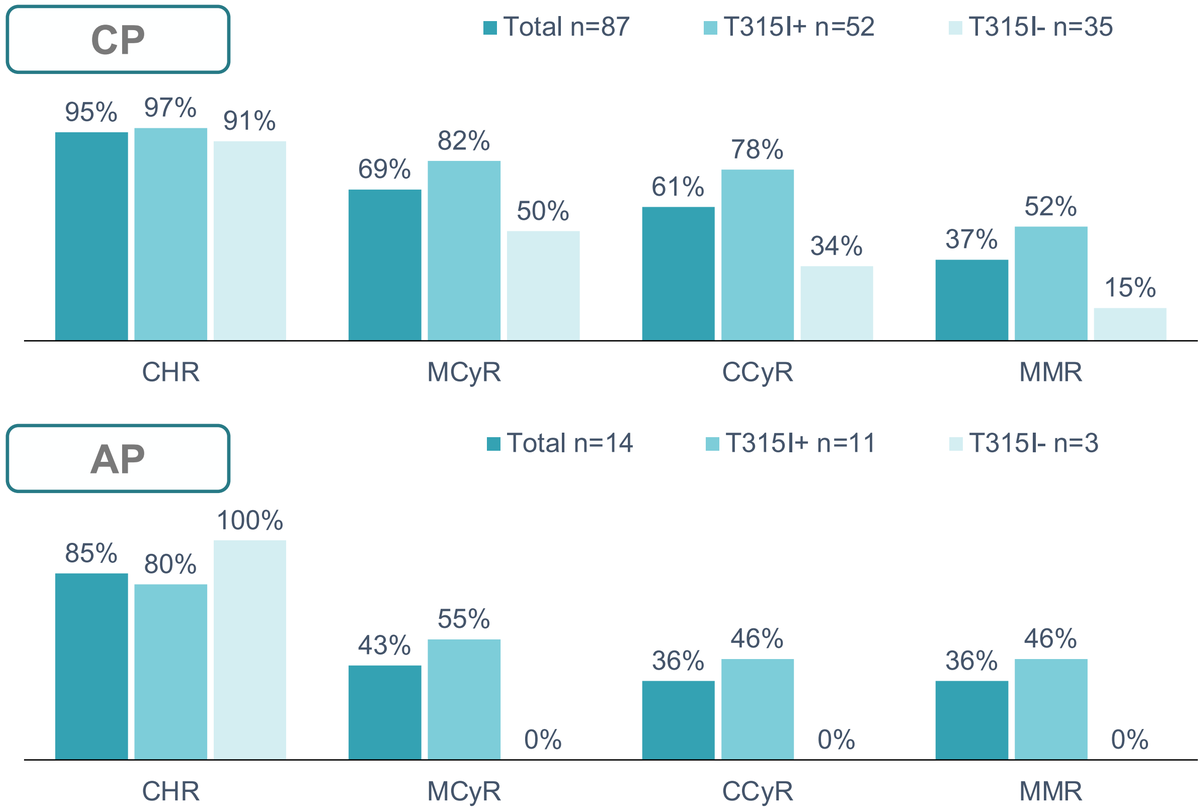
- In April, granted **Orphan Drug Designation** and **Fast Track Designation** by FDA
- In Jun, submitted **NDA** to the CDE for T315I-mutant CP-CML and AP-CML in China
- In Oct, HQP1351 has granted “**Priority Review**”

2021

- In March, received “ **Breakthrough Therapy Designation** “

Phase I Study Summary

Highly Efficacious in TKI Resistant CML Patients



CML Response Criteria: Complete Hematological Response (CHR), Bone Marrow; Major Cytogenic Response (MCyR*) Complete Cytogenic Response (CCyR), Major Molecular Response (MMR^)

* 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: **50 months**
- Average observation period: more than **2 years**; mean exposure: **30.0 months**, median exposure: **30.8 months**

Minimal Discontinuation

- Among 101 patients enrolled, **82 patients** remain on the study (since 2016)
- Most treatment-related AEs **were mild or moderate**

Much less Cardiovascular AE

- Much less 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 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

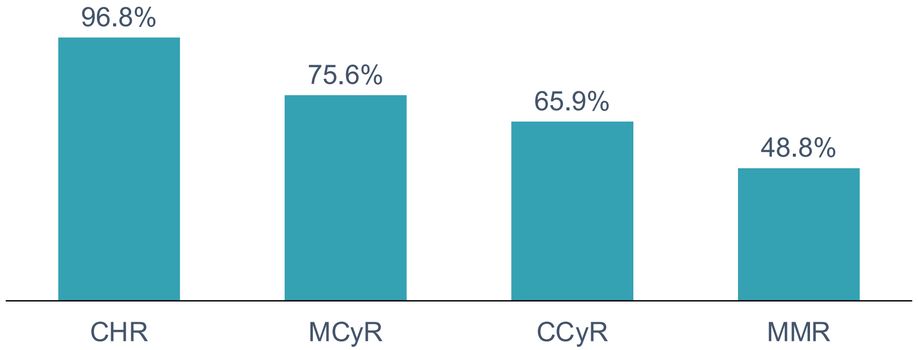
Source: Company data

Pivotal Phase 2 Study Summary

Highly Efficacious in T315I-Mutated CML Patients

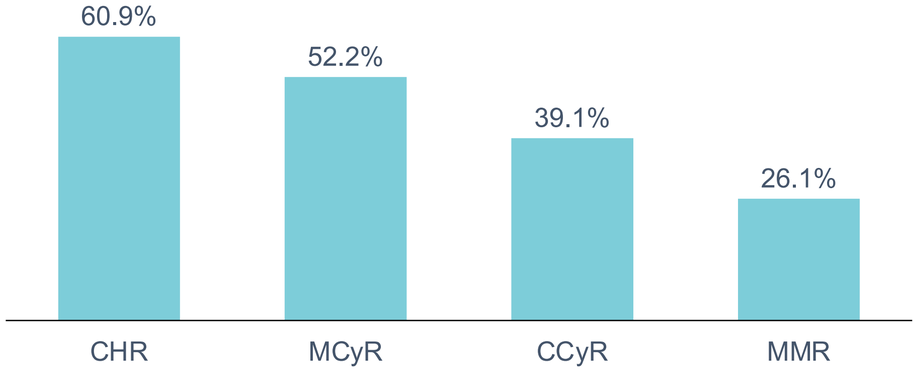
CP

T315I+n = 41



AP

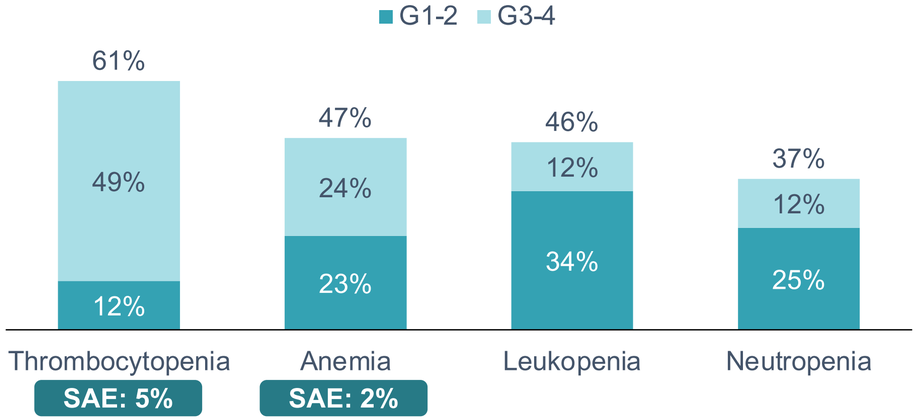
T315I+n = 23



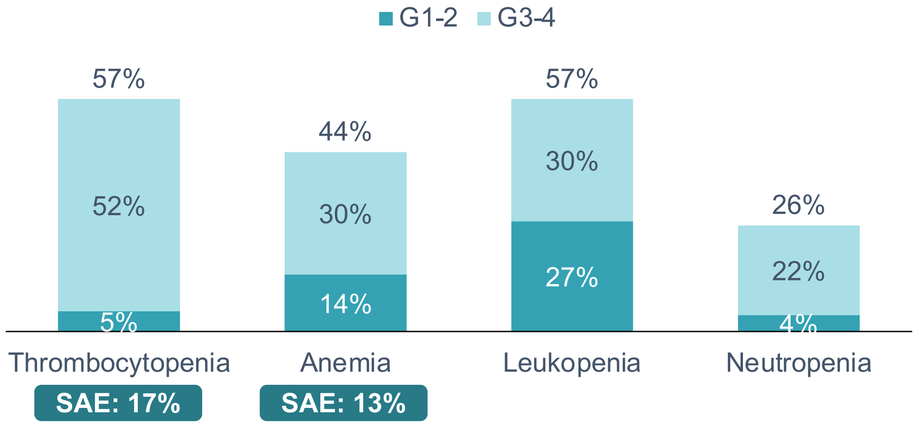
CML Response Criteria: Complete Hematological Response (CHR), Bone Marrow; Major Cytogenic Response (MCyR*) Complete Cytogenic Response (CCyR), Major Molecular Response (MMR^)

Treatment-related Hematologic Adverse Events

CP



AP



* MCyR is a validated End Point, ^ MMR defined by PCR (<1/1000)

Source: Company data

HQP1351 Development Plan

Product	Target	Region	Indications	Study		Phase I	Phase Ib	Phase II	Pivotal	NDA	Approval
HQP1351	BCR-ABL /KIT	China	CML	SJ-0002			●				
				CC201	TKI resistant CML-CP				●		
				CC202	TKI resistant CML-AP				●		Conditional Approval in 2021
				CC203	TKI resistant CML-CP				●	Enrollment completed	
		USA		CU101	PK bridging		◔ 9 pts enrolled, 100% response rate in evaluable pts				Full Approval anticipated in 2022/23
				Pivotal Trial					○	In preparation	Approval anticipated in 2023
		China	Ph+ ALL	CC204					○	Protocol submitted to CDE	

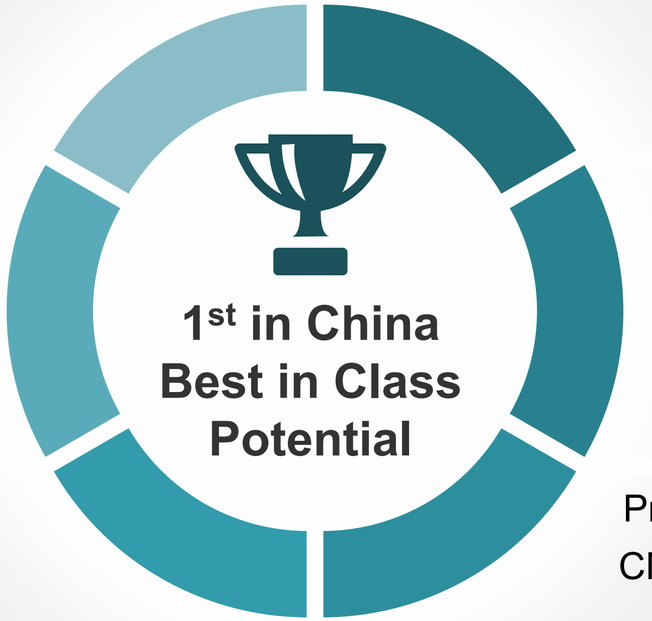
● Enrollment completed ◔ Enrollment to be completed soon ○ Enrollment not started

HQP1351: T315I and Beyond

First 3rd 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” and “Breakthrough Therapy Designation”

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



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

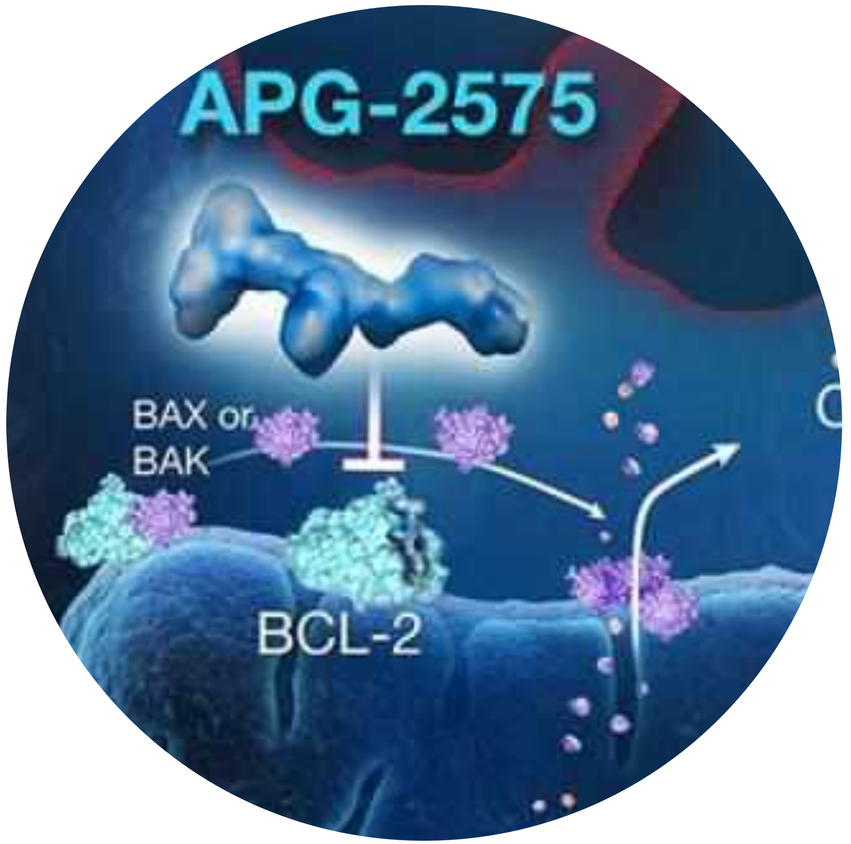
Efficacious in the patients who failed/ intolerant to ponatinib. Also active in the presence of compound mutations where ponatinib is ineffective

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

Plan to have EoP1 meeting with FDA in Q4 2021

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

	亞盛醫藥 Ascentage Pharma	abbvie
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, Breast Cancer	CLL, AML, MM, MCL, MDS, NHL, ALL, Breast cancer, Prostate cancer
Combo agents	BTK, CD20, MDM2, CD47, CDK4/6	BTK,CD20,CDK9,Pi3K, MDM2,JAK,PD-(L)1, FLT-3,IDH,CD33,CD38, CDK4/6, CD47 etc.
Comments	• Patient-friendly daily dose-ramp-up • No or Low TLS • Less risk of DDI • Less neutropenia • Strong synergy with in-house MDM2-p53 inhibitor APG-115	• NDA approved in April 2016 • First-in-class Bcl-2 inhibitor • 6 FDA Breakthrough Therapy designations • 4 approved indications across CLL and AML populations • 250+ trials across US, China, EU, Japan, etc. • Enrolled 10,000+ patients

Source: Global Data

APG-2575: IND Approval to 17 Global Phase Ib/II Studies in 3 Years

- **FDA cleared** IND for orally administered APG-2575 in patients with hematologic malignancies

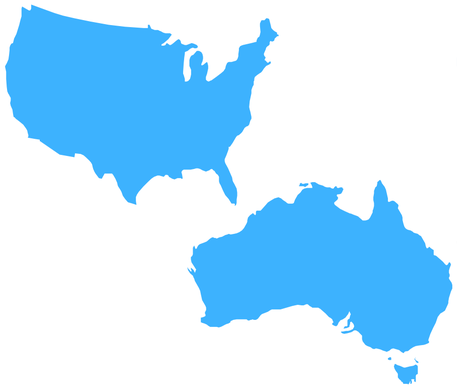
- Phase I clinical trial protocol for APG-2575 in patients with hematologic malignancies approved In Australia

- NMPA approved: An IND for APG-2575 for treatment of patients with hematologic malignancies

- **2** Phase I trial of APG-2575 in hematologic malignancies enrolling in US & AU
- **17** Phase Ib/II study for r/r AML, r/r CLL, r/r MM, r/r WM, T-PLL, HCL, DLBCL,MCL,FL, ER+ breast cancer
- **5** ODDs in AML, CLL, MM, WM, FL
- FPI in Europe

1/2018 → **6/2018** → **10/2018** → **11/2020**

3 Phase Ib/II studies in r/r CLL/SLL in Europe



1 Phase 1 in US/AU

6 Phase Ib/II studies in r/r CLL/SLL, MM, WM, AML, T-PLL, ER+ breast cancer and other solid tumors in US/AU

1 Phase 1 in China

6 Phase Ib/II studies in r/r AML, r/r CLL/SLL, WM ,MM, T-PLL, ER+ breast Cancer and solid tumors in China

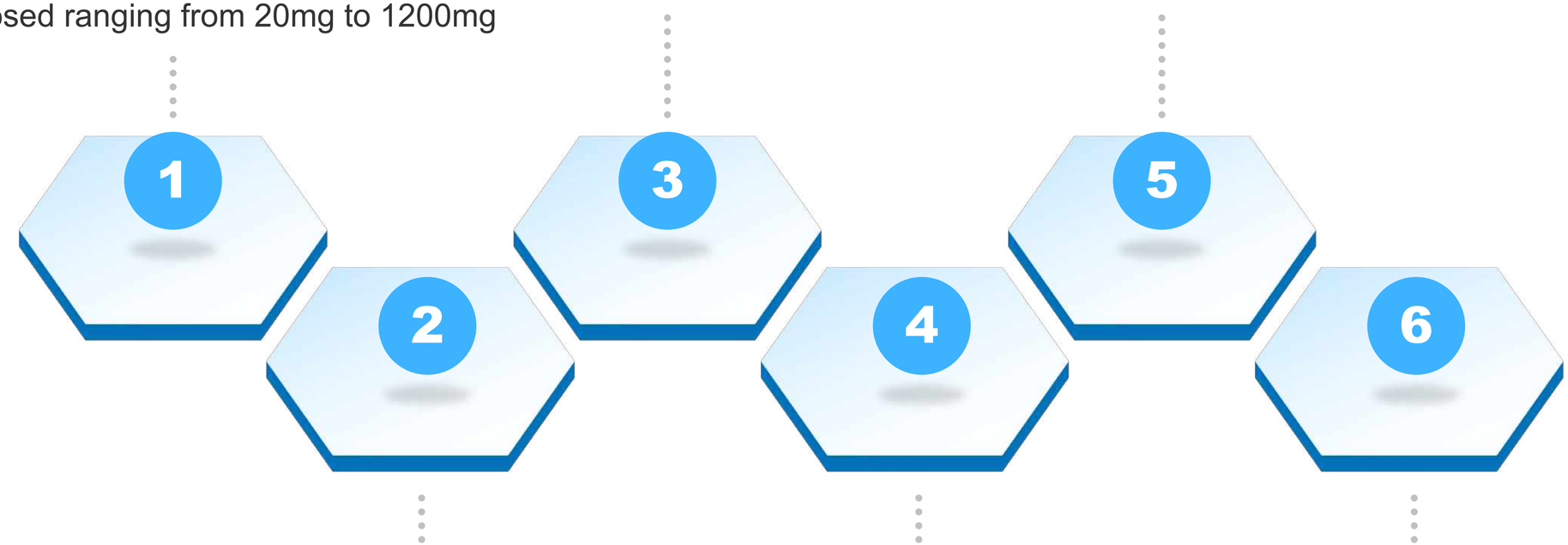
Source: Company data

Clinical POC Established With Best-in-Class Safety Potential

More than **150 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

Potential Best-in-Class Safety Profile: Less TLS, no DLT, no MTD reported

IND clearance for ER+ breast cancer and other solid tumors



Proof of Concept established in r/r CLL, more than 50 pts enrolled; 80% evaluated pts achieved PR as of April 15th 2021

5 Orphan Drug Designations (ODD): CLL, WM, MM, AML, FL

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

Source: Company data

Safety/tolerability profile

Treatment-related adverse events (TRAEs) with APG-2575 (N = 36)

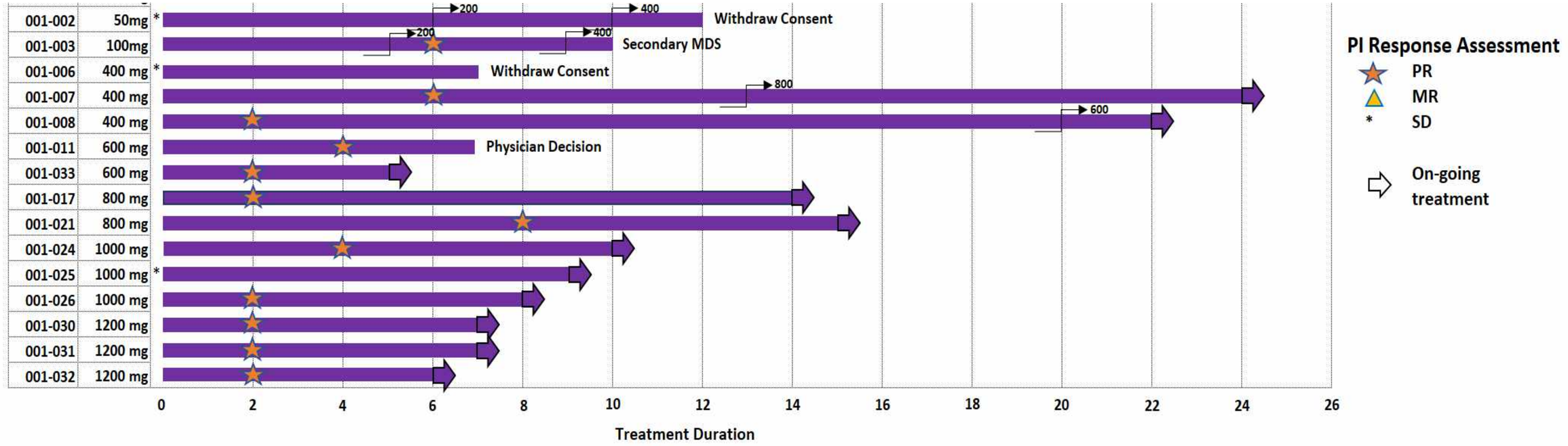
Any grade AE (≥ 10%)	No. (%)	≥ Grade 3 AE (≥ 5%)	No. (%)
Any APG-2575-related AE[a]:	27 (75.0)	Any ≥ grade 3 APG-2575-related AE:	9 (25.0)
Fatigue	10 (27.8)	Neutropenia	5 (13.9)
Neutropenia	8 (22.2)	Nausea	2 (5.6)
Diarrhea	7 (19.4)	Platelet count decreased	2 (5.6)
Anemia	6 (16.7)	–	–
Constipation	4 (11.1)	–	–
Nausea	4 (11.1)	–	–

- No DLTs have been observed at APG-2575 doses of up to 1,200 mg.
- The MTD has not been reached.
- No laboratory or clinical TLS has been reported during this study.
- The median (range) treatment duration is 6 (1-24) cycles.
- In Cohort B (high-risk TLS group), APG-2575 at 600 mg daily has been selected as the RP2D based on clinical results and PK/PD profile.
- In all, one patient (1/36, 2.8%) discontinued APG-2575 because of TRAEs (grade 2 pruritus, skin sensitivity).
- No grade 5 TRAEs noted.

[a]A patient with more than one AE is counted once.

80% PR in Evaluable R/R CLL/SLL Patients

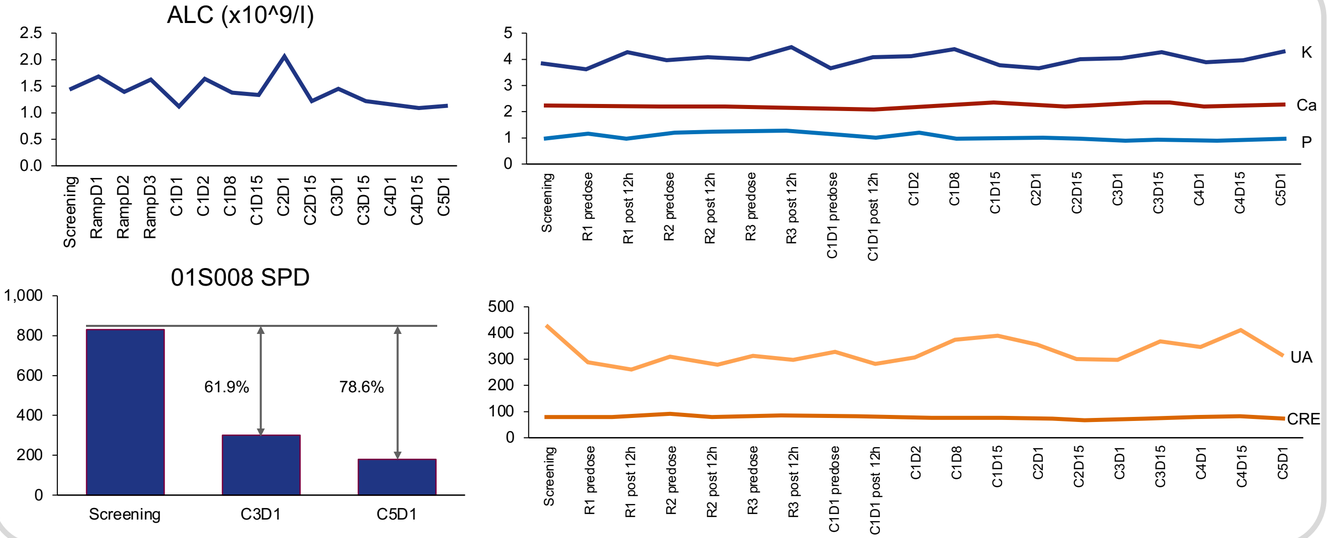
CLL/SLL Swimmer Plot



Source: Company data

APG-2575-CN-001 Phase I Interim Data I Efficacy

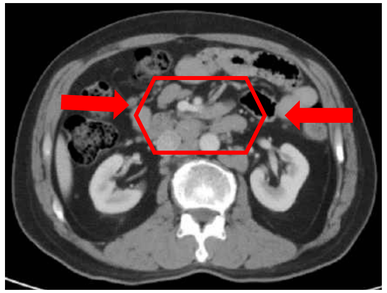
Ibrutinib Resistant High Risk Patient; Rapid and Deep Response



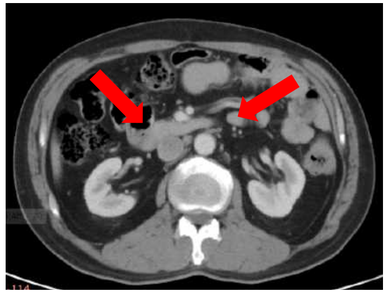
Patient 1S008: -78.6% Nodal Response

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

Before APG-2575



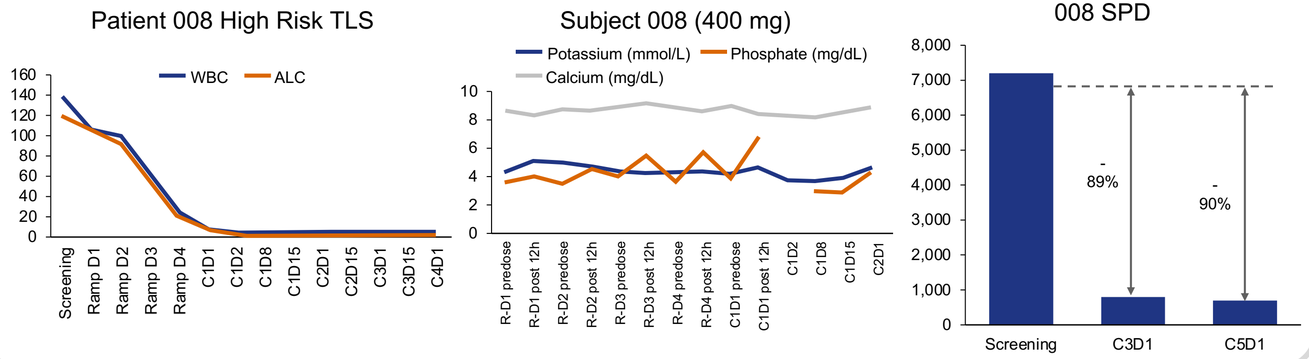
After APG-2575



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

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

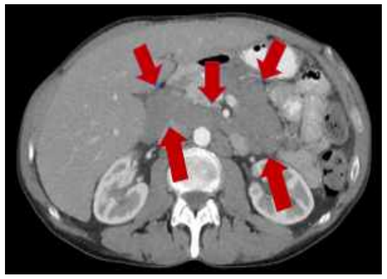
Patient 008: PR parameters



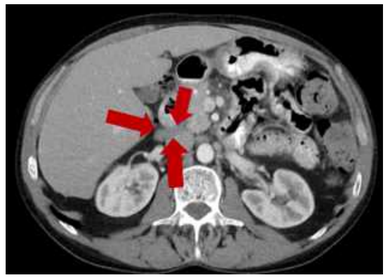
Durable PR in a patient with r/r CLL

Patient 008: -90% Nodal Response

Before APG-2575



After APG-2575

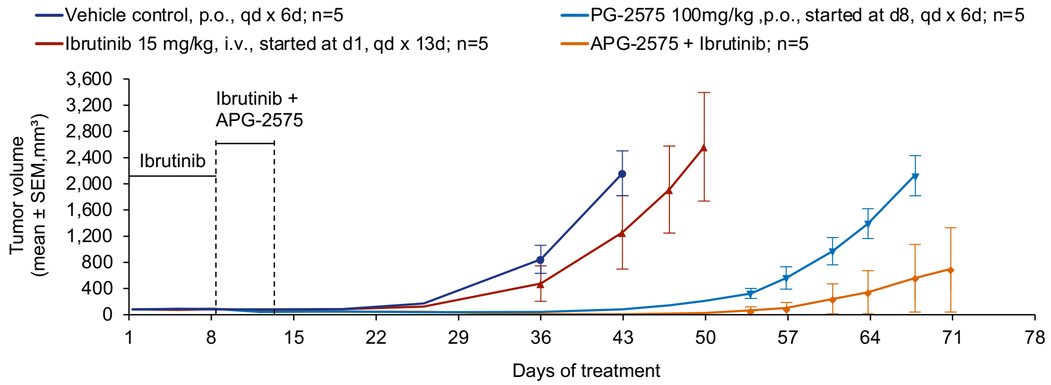


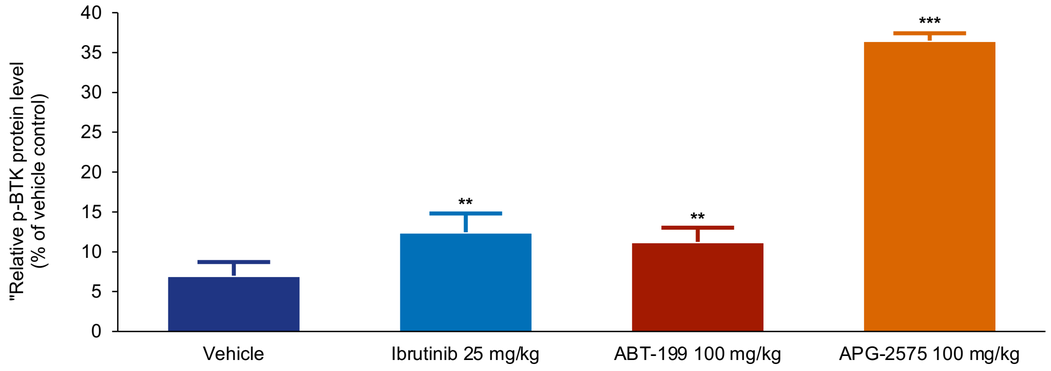
Nodal Response: C3D1-89% | C5D1-90%

Source: Company data

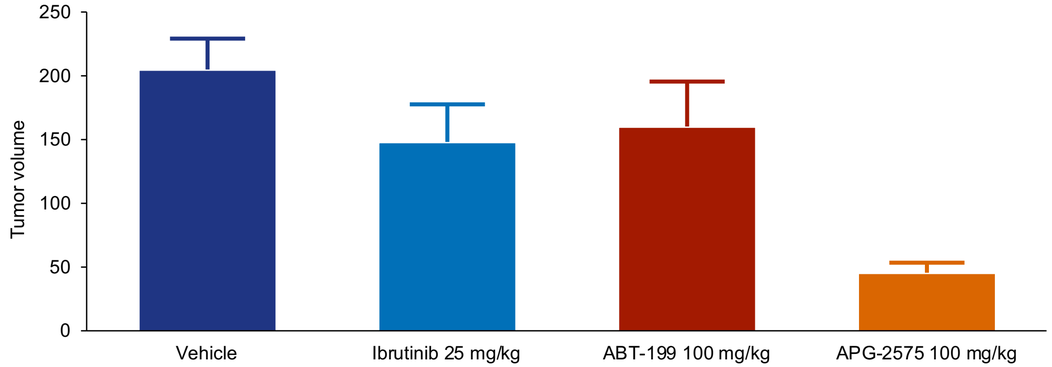
Strong Pre-clinical Data in BTK Combo and BTK Resistant Pts

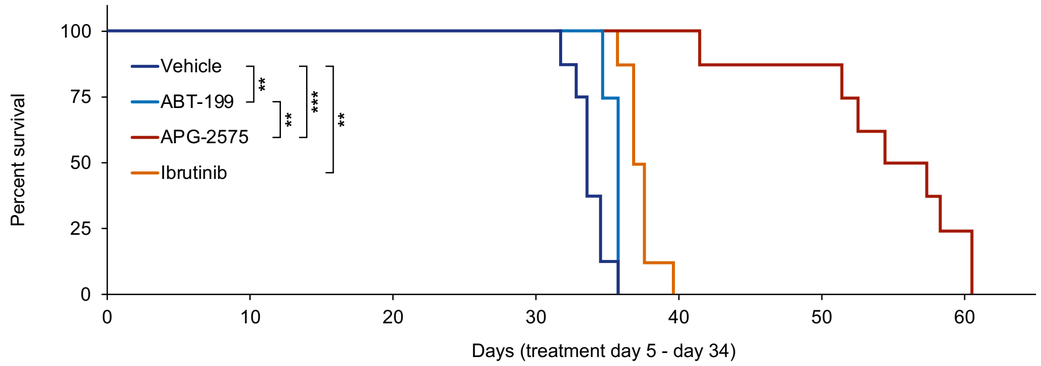
Synergistic Effects of APG-2575 in Combination with Ibrutinib





Efficacious In BTK Resistant WM PDX Model In Which Venetoclax Shows No Activity





Source: Company data

Strong Differentiation From Venetoclax

APG-2575 Compared to Venetoclax

- Efficacious in BTK resistant WM PDX model in which Venetoclax shows no effect
- Daily ramp-up verse weekly ramp up
- Low lab and clinical TLS
- Less neutropenia and thrombocytopenia
- Short T1/2 & exposure--potentially lower risk of TLS with better safety profile

Conclusion

When Selectively Targeting BCL-2

Less is more

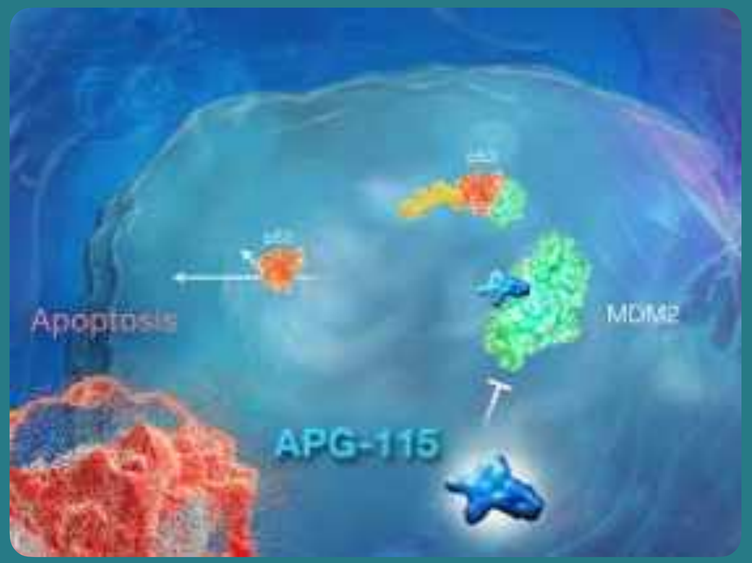
- Dose Escalation (Daily Ramp)
- PK Properties (T1/2 & AUC)
- Safety: TLS, DDI

Source: Company data

APG-115 Overview

MDM2-p53 Inhibitor

Activates p53 tumor suppression via MDM2-p53 PPI



Milestones & Clinical Developments

- Granted ODD for the treatment of AML, gastric cancer ,soft tissue sarcoma, retinoblastoma and stage IIb to IV melanoma
- China: the first MDM2-p53 inhibitor entering clinical stage in China, with multiple ongoing clinical studies in treating solid tumors as well as hematological tumors.
- U.S: enrolling three clinical trials of APG-115.
- A Phase Ib/II study in combination with pembrolizumab for treatment of metastatic melanoma and other advanced solid tumors, in collaboration with Merck
- A Phase I/II combination with chemo in AML
- A Phase I/II study as a single agent or in combination with chemotherapy for treatment of salivary gland cancer.
- 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.

- Blocks MDM2-P53 PPI & activates the tumor suppressor P53
- Directly regulates host immunological responses in the TME and potentially overcome IO resistance
- Effectively induces apoptosis with the best-in-class potential
- Synergy with PD-1 blockade in both TP53WT and TP53MUT tumors
- MDM2amp associated with Hyperprogression after αPD1 Rx (Kato et al., 2017)

Initial Signs of Efficacy in IO combo

Phase Ib Study in IO resistant/relapsed patients in combination with Keytruda®

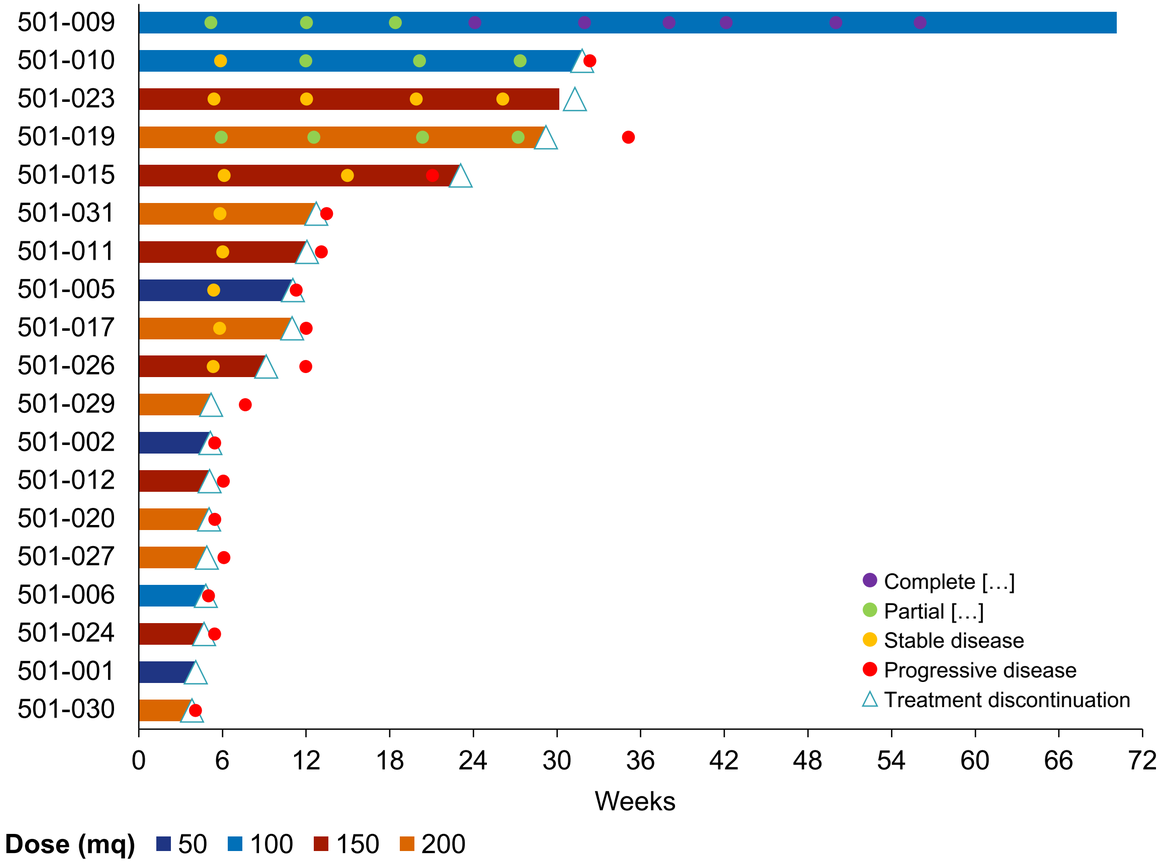
Overview & Safety

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 safety 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.
- Efficacy: **ORR: 16.7%** (1 CR|2PR) + 7SD = **DCR: 55.5%**
  - Resp: CR-Ovarian| PR-NSCLC, Appen. Adeno.|7SD | 8PD

Overview & Treatment Duration



Source : American Society of Clinical Oncology (ASCO),
Virtual Scientific Program, May 29-31, 2020, Abstract Number: #3512

Efficacy in IO Combo

Phase II Study in multiple cohorts in combination with Keytruda®

Efficacy in all Cohorts

Response	Melanoma (n = 32)	NSCLC (n = 19)	STK-11 (n = 5)	ATM (n = 11)	Liposarcoma (n = 17)	UC (n = 12)	MPNST (n = 6)
ORR (CR + PR)	24.1% (7/29)	6.7% (1/15)	0	0	6.2% (1/16)	12.5% (1/8)	16.7% (1/6)
DCR (CR + PR + SD)	55.2% (16/29)	46.7% (7/15)	25% (1/4)	44.4% (4/9)	81.2% (13/16)	12.5% (1/8)	66.7% (4/6)
Best overall RECIST or iRECIST response							
CR	1	0	0	0	0	0	0
PR	6 (2 unconfirmed)	1	0	0	1 (unconfirmed)	1	1 (unconfirmed)
SD	9	6	1	4	12	0	3

- ORR and DCR are based on efficacy evaluable population; stable disease (SD) requires a minimum duration of 2 cycles.
- CR, complete response; DCR disease control rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; UC, urothelial carcinoma.

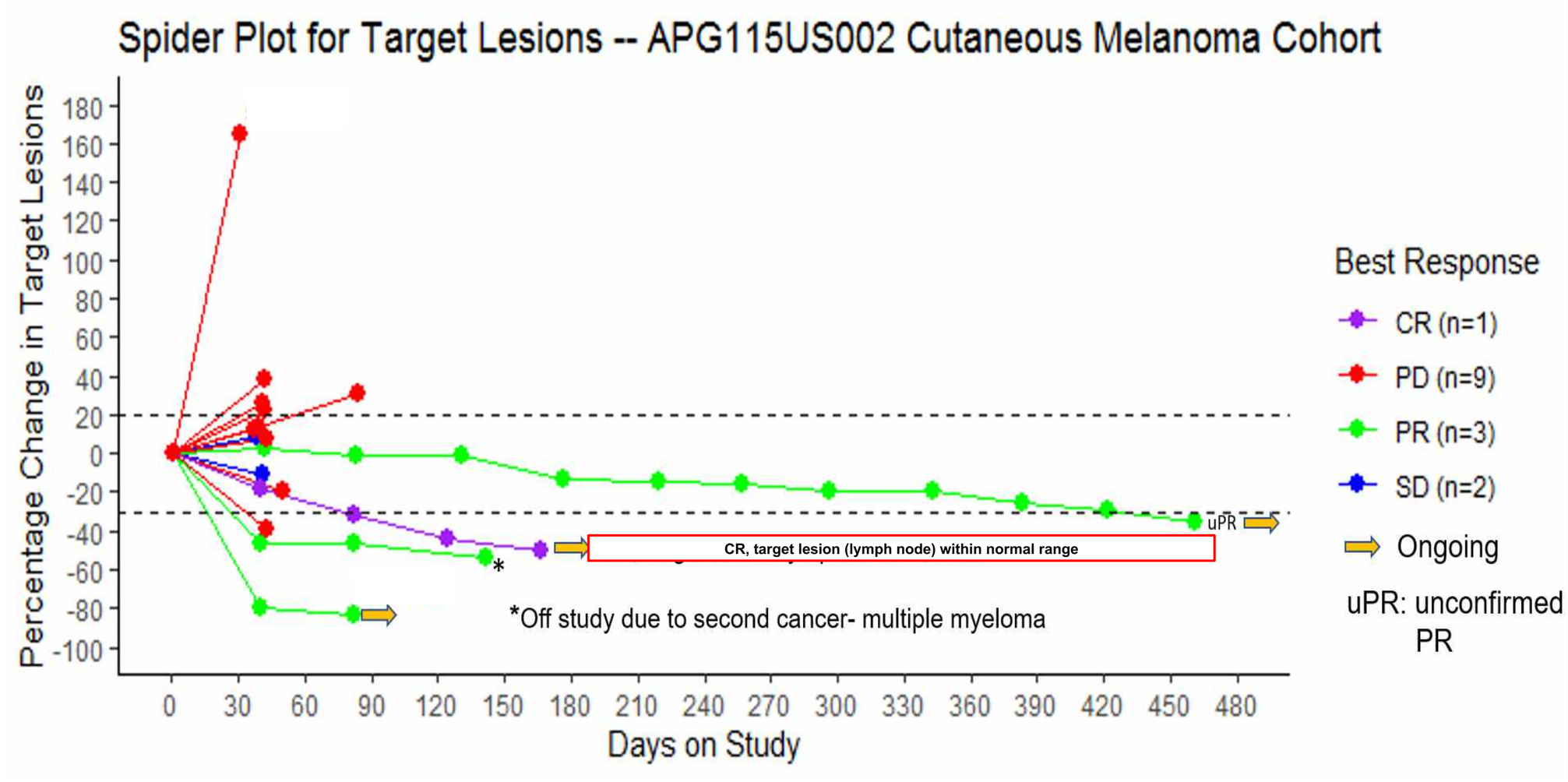
Efficacy in Patients with IO Resistant Melanoma

Response	Uveal (n = 8)	Mucosal (n = 5)	Cutaneous (n = 16)	Unknown primary (n = 3)	Total (N = 32)
ORR (CR + PR)	14.3% (1/7)	40% (2/5)	26.7% (4/15)	0	**24.1%** (7/29*)
DCR (CR+ PR+ SD)	71.4% (5/7)	40% (2/5)	46.7% (7/15)	100% (2/2)	**55.2%** (16/29)
Best overall RECIST or iRECIST response					
CR	0	0	1	0	**1**
PR	1	2 (1 unconfirmed)	3 (1 unconfirmed)	0	**6**
SD	4	0	3	2	**9**

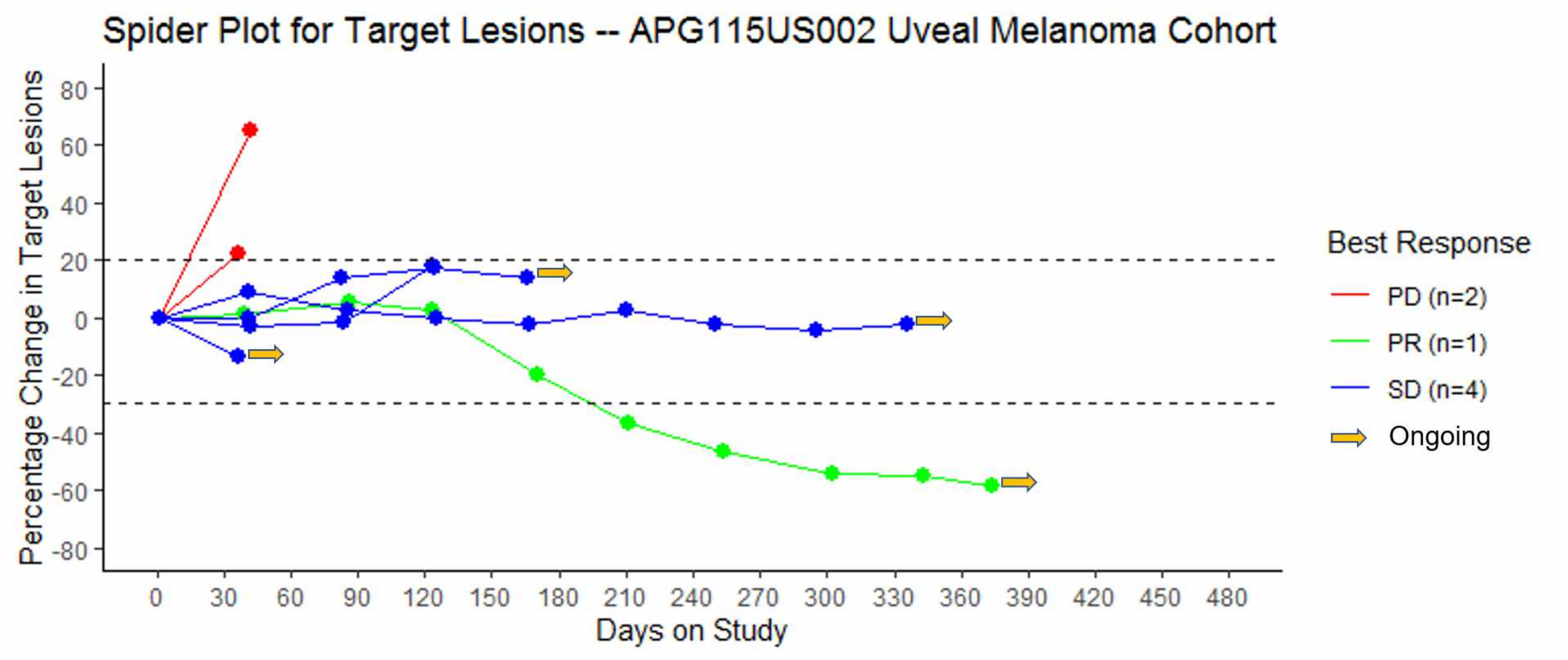
Data cutoff: April 15, 2021

* Total evaluable patient N: 29

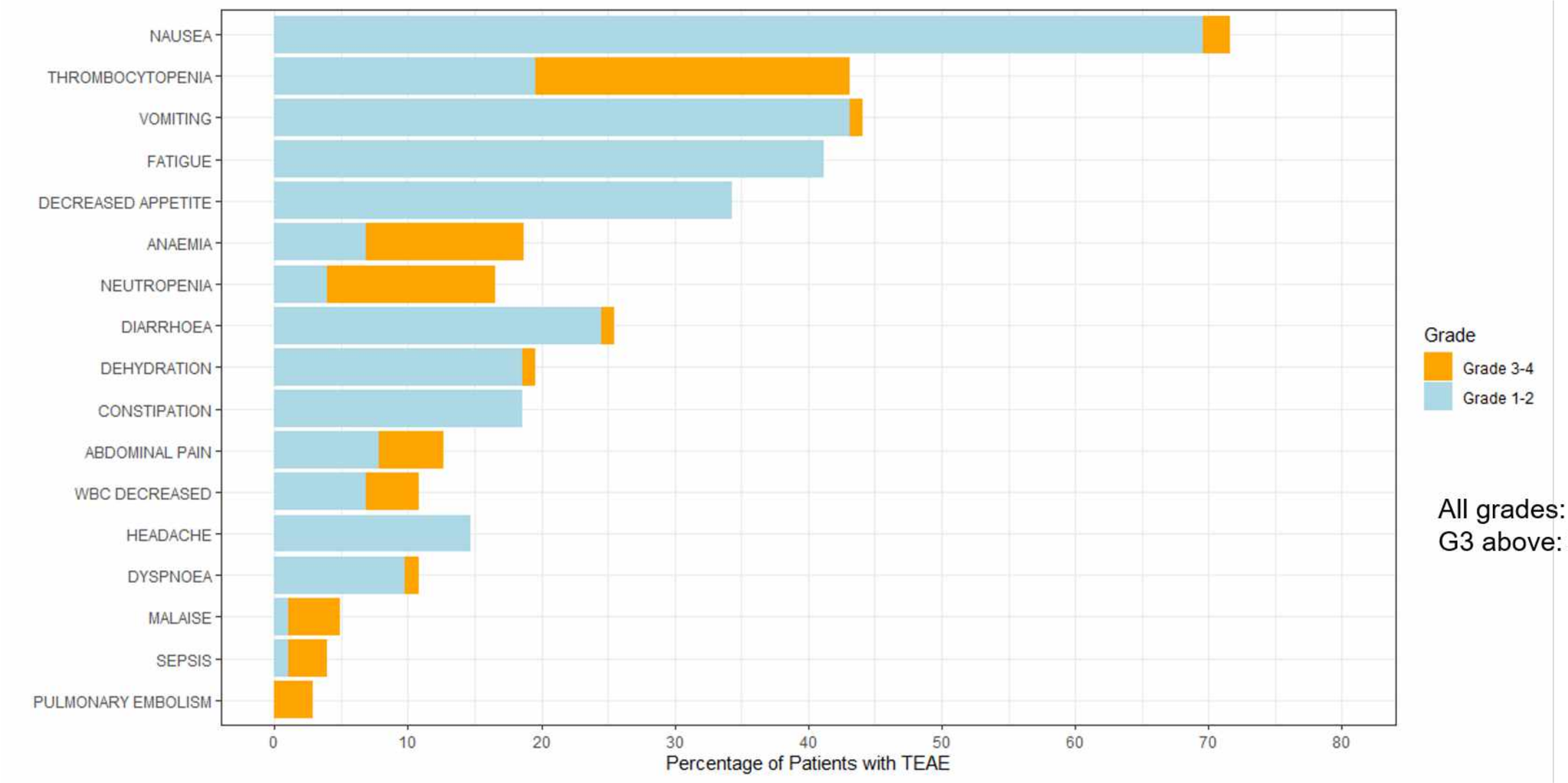
Efficacy in Patients with IO Resistant Cutaneous Melanoma Treated with APG-115 Plus Pembrolizumab



Efficacy in Patients with IO Resistant Uveal Melanoma Treated with APG-115 Plus Pembrolizumab



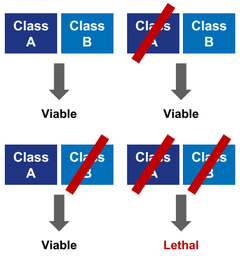
Safety: Treatment Emergent AEs (TEAEs)



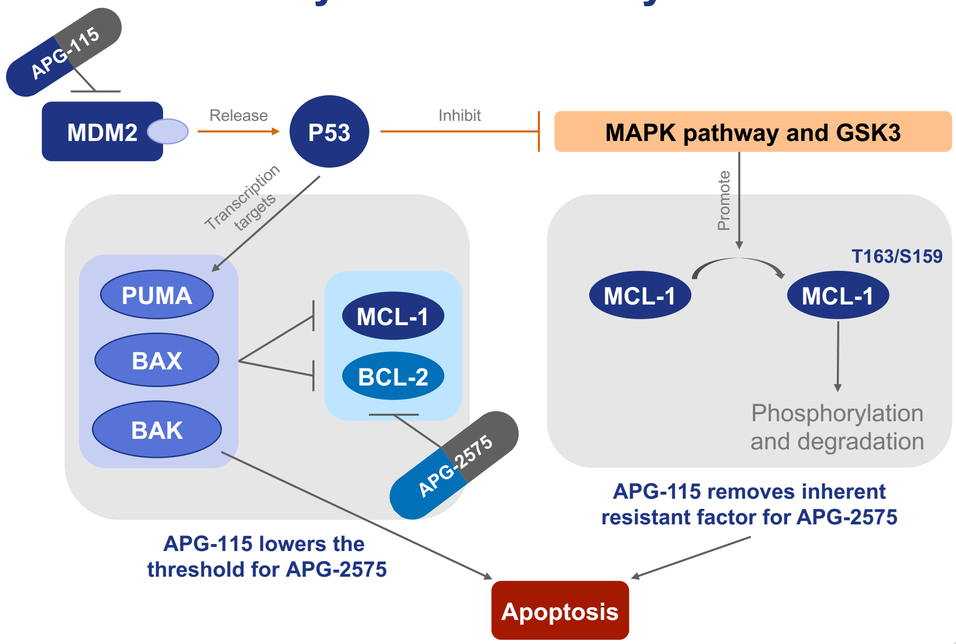
All grades: ≥ 10%
G3 above: ≥2%

Combining APG-115 and APG-2575 to Achieve Synthetic Lethality

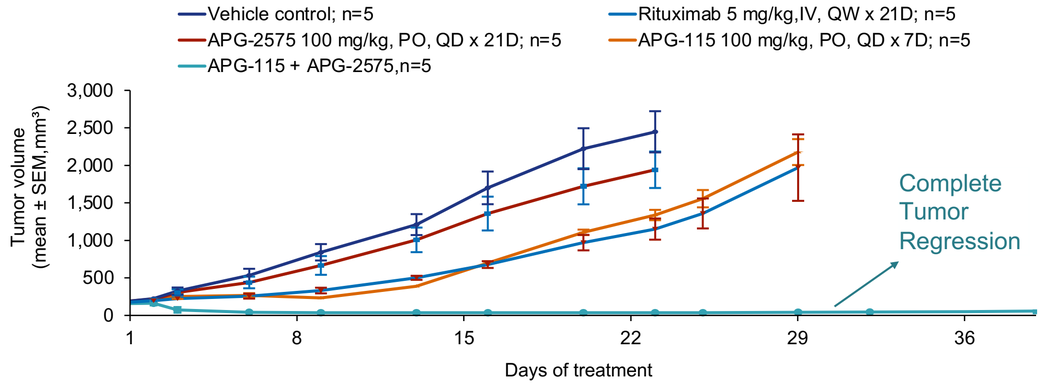
- **“Synthetic lethality”** describes a strategy where blocking two mutations result in cell death, but the cancerous cells only has one mutation. By artificially inducing a second mutation the medicine can induce cancerous cell death.

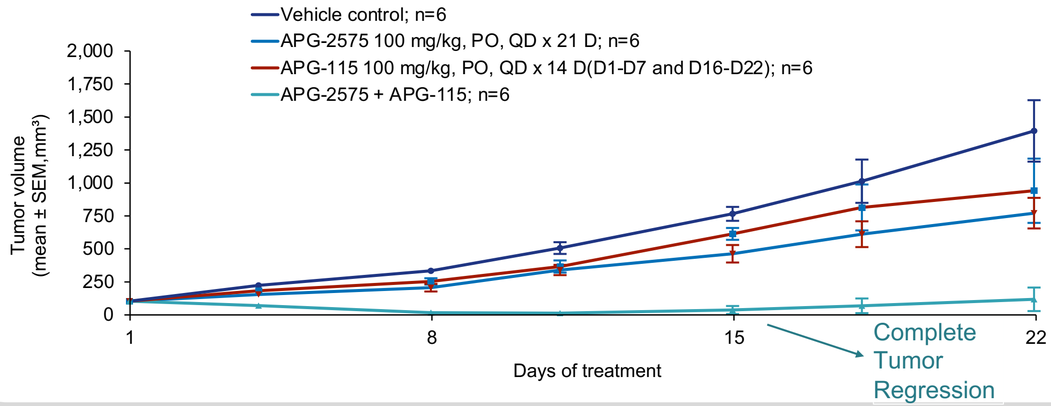


Synthetic Lethality



Complete Response in Animal Tumor Models



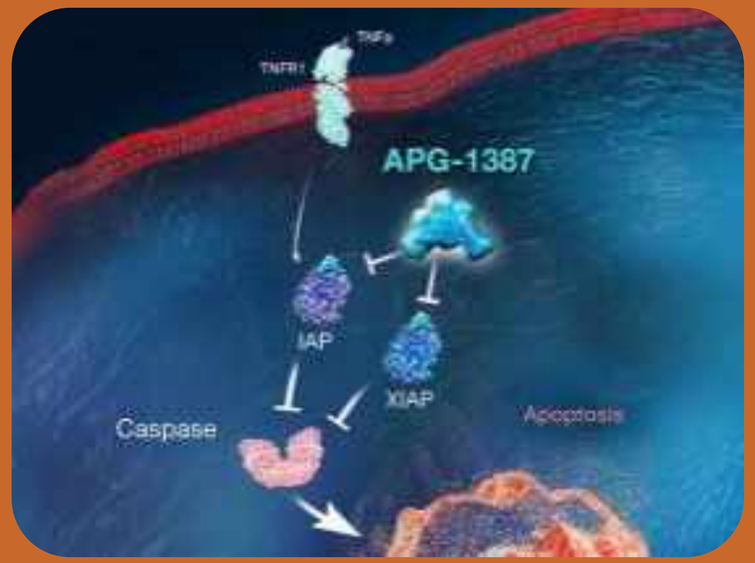


Use in Both Heme and Solid tumors , both oral and Chemo- Free, 1 + 1 > 2!

Source: Company data

APG-1387

An Antagonist of IAP/XIAP
(SMAC Mimetic) Dimmer



Immuno-Oncology Development

- Only SMAC mimetic to inhibit both IAP1/2 and XIAP in the clinic
- Completed **3** Oncology Phase-1 dose escalation trials; known MTD and RP2D; AEs were mild to moderate, manageable and reversible
- Preliminary efficacy signal seen in combination with pembrolizumab, no additive toxicity
- **2** Phase Ib/II clinical trials of APG-1387 combined with immuno-checkpoint inhibitor or chemotherapy in advance solid tumors are ongoing

CHB Developments

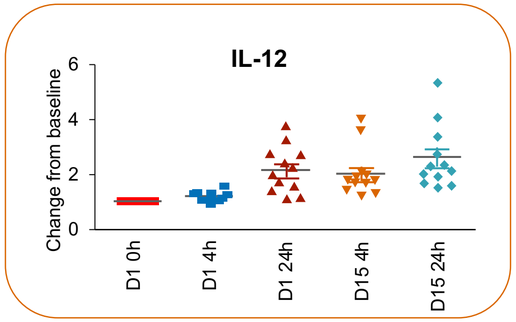
- A Phase Ib trial in naive Chronic Hepatitis B (CHB) patients completed the enrollment
- A Phase Ib/II trial combo with NAs in CHB patients is ongoing

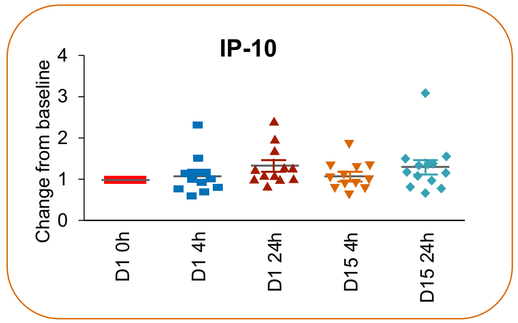
Initial Signs of Efficacy in IO Combo

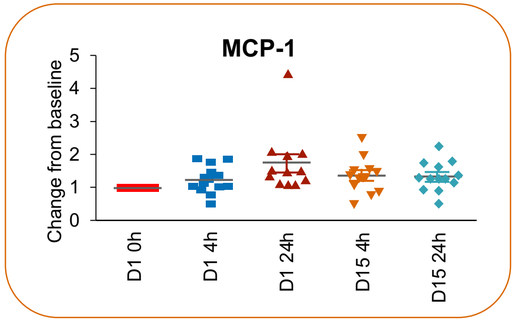
Phase Ib IO resistant/relapsed patients| combination with pembrolizumab

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 tumor types (N=56)	NSCLC (n=16)	Colorectal cancer (n=9)	Breast cancer (n=10)	HNSCC (n=3)	Ovarian cancer (n=7)	Pancreatic (n=7)	Others (n=4)
ORR (objective response rate, CR+PR)	12.0% (6/50)	15.4% (2/13)	11.1% (1/9)	11.1% (1/9)	33.3% (1/3)	16.7% (1/6)	0	–
DCR (disease control rate, SD and above)	50.0% (25/50)	92.3% (12/13)	44.4% (4/9)	33.3% (3/9)	33.3% (1/3)	50% (3/6)	16.7% (1/6)	–
Best overall response, n								
CR	0	0	0	0	0	0	0	0
PR	6	2	1	1	1	1	0	0
SD	20	10	3	2	0	2	1	2
PD	24	1	5	6	2	3	5	2
Non-evaluable	5	2	0	1	0	1	1	0
Not assessed	1	1	0	0	0	0	0	0

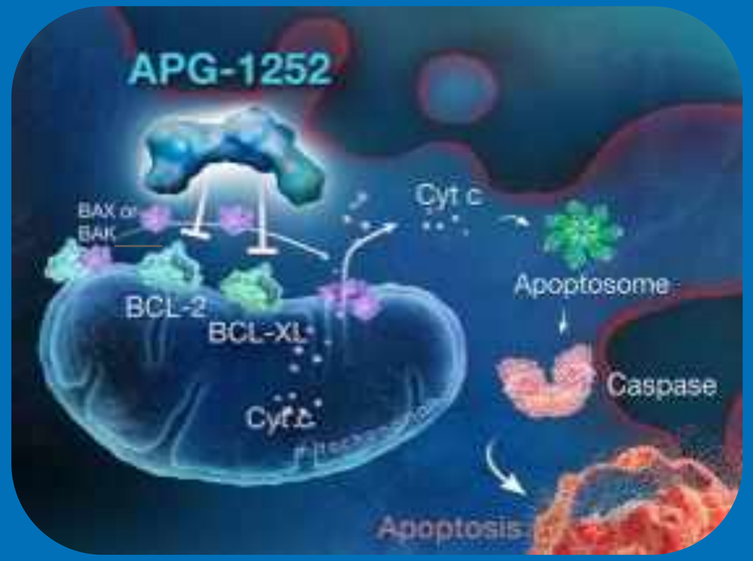
Among 50 efficacy evaluable patients;

- ORR 12% | 6-PR (2 NSCLC |1 CRC |1 BC |1 HNSCC |1 ovarian cancer)
- DCR 50% | 20- SD
- All TRAE were grade 3. No grade 4 and above TRAE were observed

Source : American Society of Clinical Oncology (ASCO), Virtual Scientific Program, May 29-31, 2020, Abstract Number: #3512

APG-1252
Pelcitoclax

BCL-2/BCL-xL Inhibitor



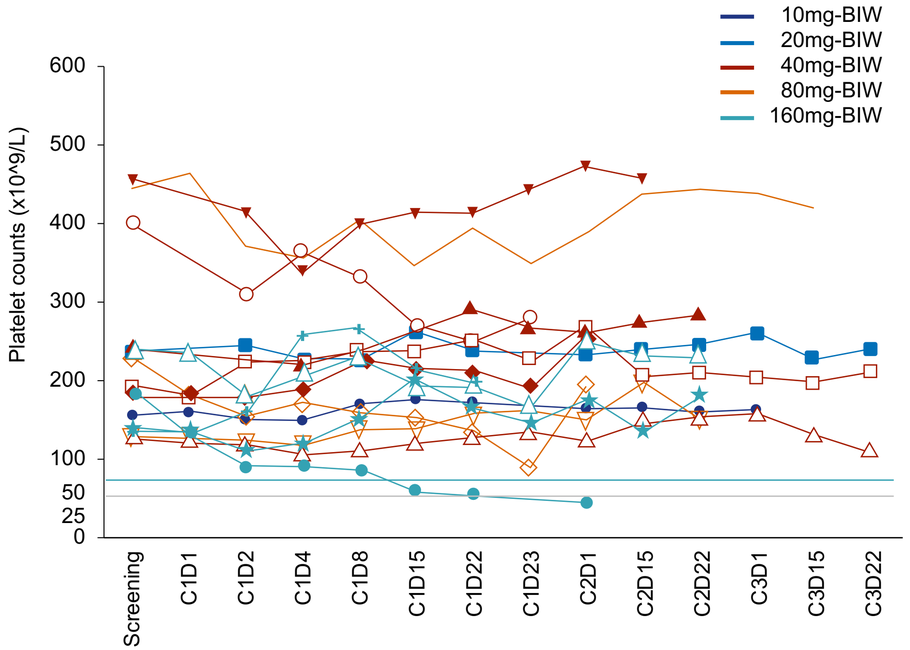
Milestones & Clinical Developments

- Potentially the best-in-class Bcl-2/Bcl-xL inhibitor with novel combination in solid and hematological malignancies
- Entered 2 combination trials
  - A Phase Ib/II study of APG-1252 plus Ruxolitinib in patients with myelofibrosis in the United States
  - A Phase Ib study of APG-1252 plus Osimertinib in patients with NSCLC in China
- A total of 183 patients have been treated with APG-1252
- Granted ODD for the treatment of SCLC in Sep 2020

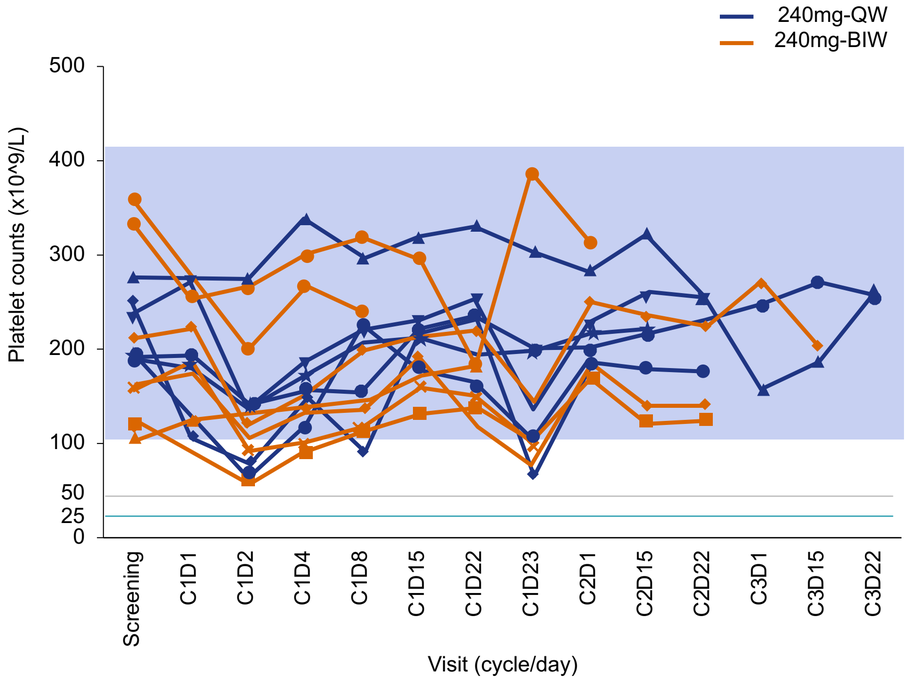
APG-1252 Phase I Safety Data: Well-Managed Platelet Toxicity

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

APG-1252
10-160mg dose cohorts



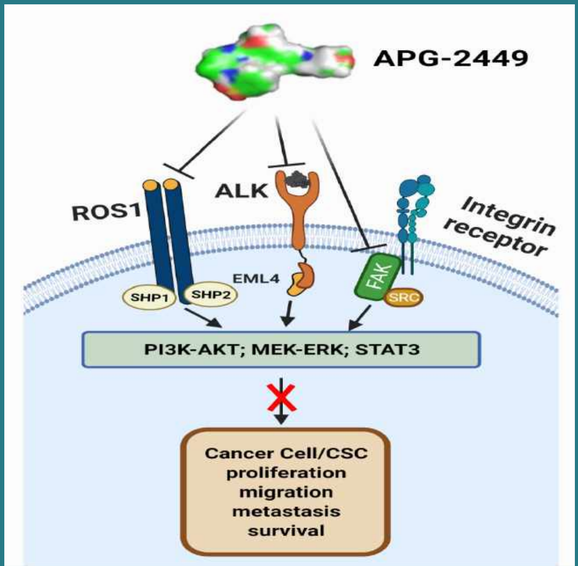
240mg dose cohort
(N=13)



Source : American Society of Clinical Oncology (ASCO),
Virtual Scientific Program, May 29-31, 2020, Abstract Number: 3509,

APG-2449

ALK/FAK/ROS1



Milestones & Clinical Developments

- APG-2449 is a next-generation novel potent kinase inhibitor with multiple targets including FAK, ALK and ROS1 proteins
- APG-2449 demonstrated effectiveness in multi-tumor type models as monotherapy or in combination with other agents in pre-clinical studies
- Phase I study is ongoing in China with 7 dose levels investigated,54 patients dosed as of Aug. 23rd

Pre-Clinical Assets

EED Selective/MDM2-p53 Degrader

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

High unmet medical needs

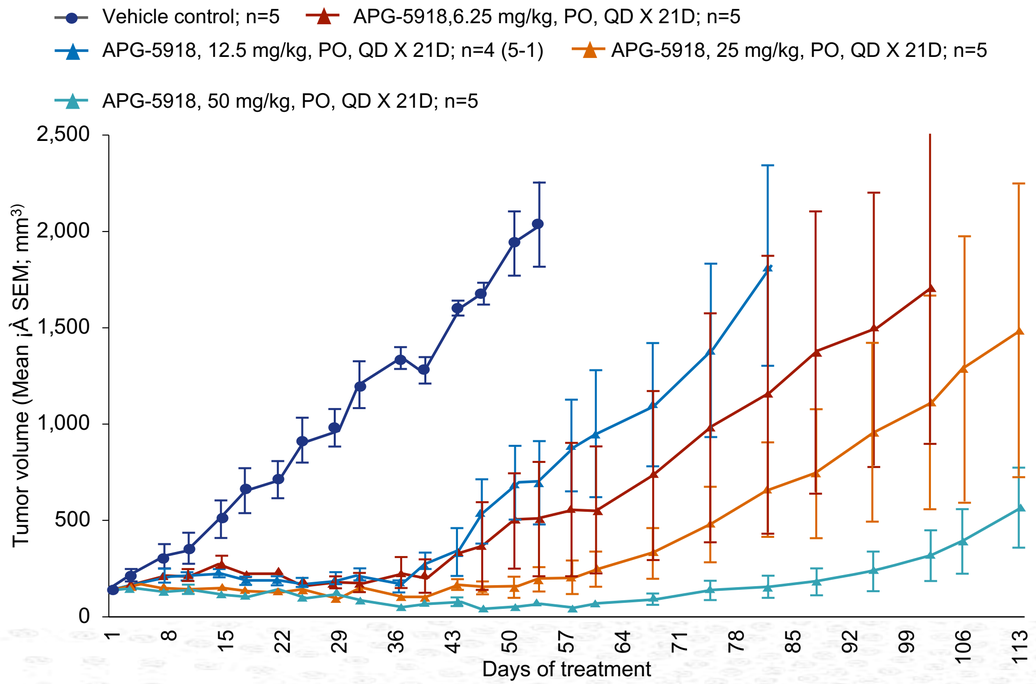
First-in-class or best-in-class potential

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_{50} (nM))		1.2	34 ± 18 (EED226)
Cell Growth Inhibition Assay (IC_{50}, nM)	Karpas422	1.94±0.6	3.3
	Pfeiffer	0.14	0.7

In vivo activity (KARPAS-422 xenograft)



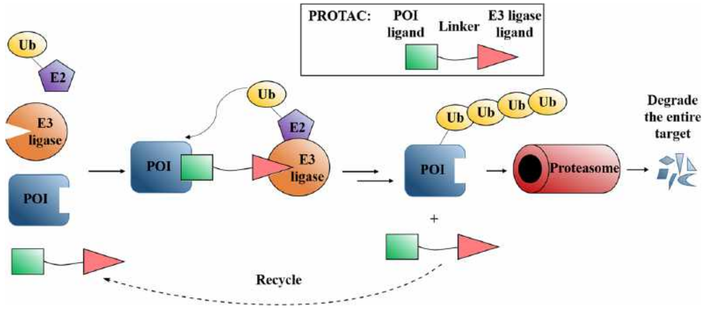
APG-5918

- A highly potent EED inhibitor
- Excellent ADME and oral PK properties
- Achieve tumor regression with oral dosing
- Well tolerated in animals
- Best-in-class potential
- EED inhibitors have achieved preclinical POC results with the potential to treat solid and hematological malignancies, as well as sickle cell disease and beta-thalassemia
- **IND-enabling studies**

Source: Company data

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 efficacy over traditional drugs (overcoming drug resistance)
- Reduced off-target toxicities
- Dramatically expanding druggable genome;

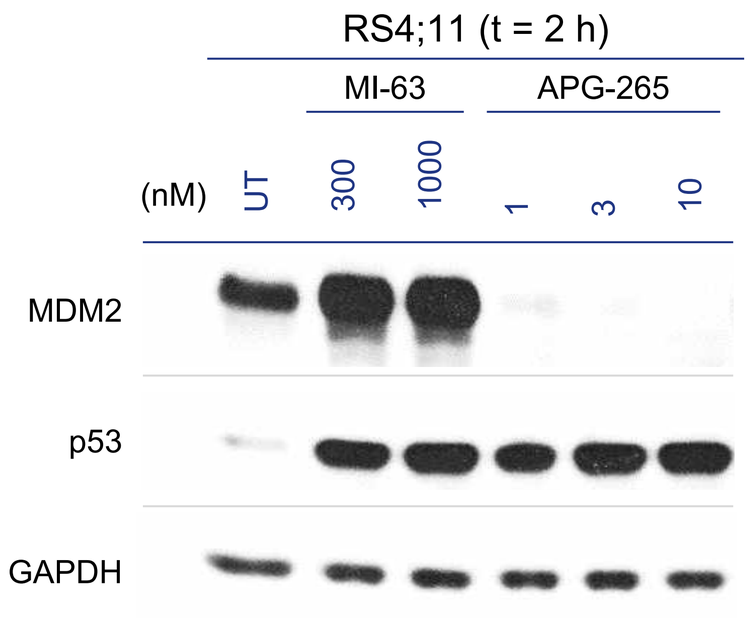
PROTACs MDM2 protein degrader

- The molecule is well-tolerated in mice, rats and dogs;
- The molecule has excellent pharmacokinetics in rodents and non-rodents

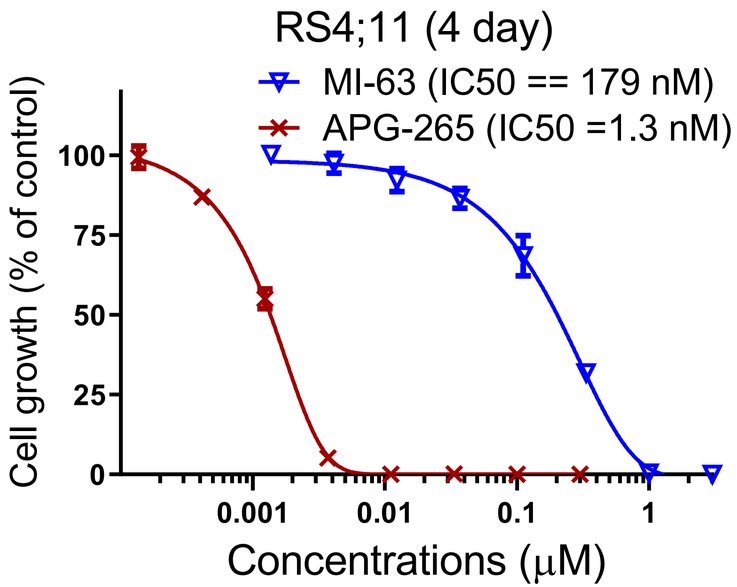
Source: Company data

PROTAC MDM2 Degrader

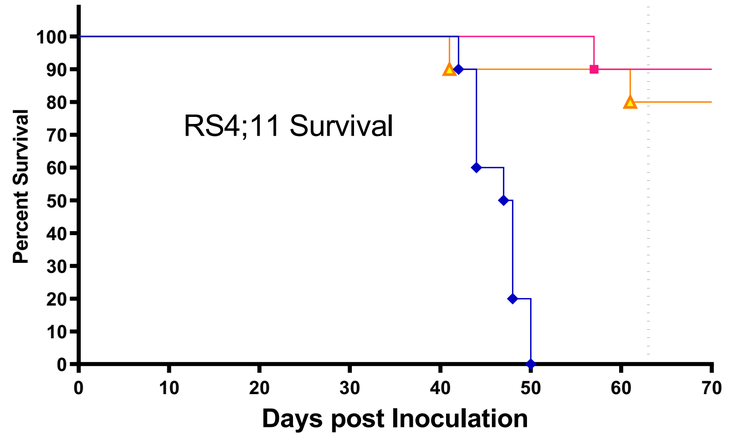
Potent and complete degradation of MDM2 protein in acute leukemia cells



>100-fold improved cell growth inhibition activity by the molecule over MDM2 inhibitor MI-63



Dramatic survival benefit in disseminated leukemia mouse model



P-value vs Control		median survival (days)
	Control 0mg/kg, IV qW	47.50
<0.0001	APG-265 25 mg/kg, IV qW	>63
0.0011	APG-265 50 mg/kg, IV qW	>63

- **The molecule :**
  - Is >100-times more potent than MDM2 inhibitor in >100 AML patient samples with wild-type p53 status
  - Is well-tolerated in mice, rats and dogs
  - has excellent pharmacokinetics in rodents and non-rodents

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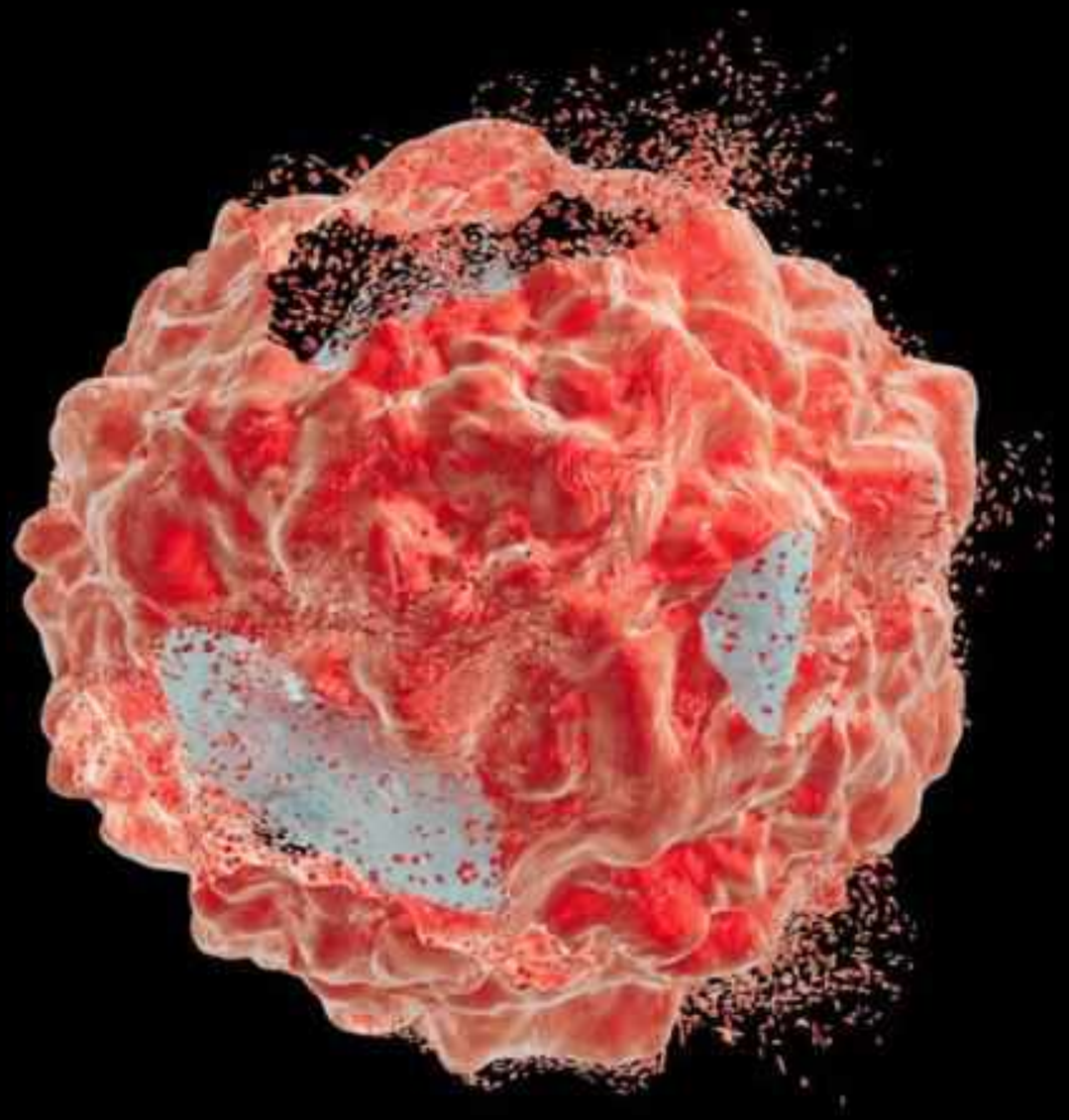
IP Portfolio for Key Clinical Assets

Core Compound	Patent Type	Year Patent Expires
HQP1351	Product (Core compound structure); Process; Combination; Use; Formulation	2031-2039/40*
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*
APG-1252	Product (Core compound structure)Process; Formulation; Combination; Use	2034-2039/40*

*some patent types are still in the prosecution process

Source: Company data Note: All data as of December 31, 2019



Ascentage Pharma Group

Advancing Therapies That Restore Apoptosis