Early clinical activity from the phase 1 evaluation of CID-078, a novel cyclin A/B RxL inhibitor, in patients with advanced solid tumors

Afshin Dowlati[1], Timothy A Yap[2], Antonio Giordano[3], Nehal Lakhani[4], William B McKean[5], Ildefonso Ismael Rodriguez Rivera [6], Vivek Subbiah[7], Kyaw Thein[8], Judy S. Wang[9], Jinshu Fang[10], Li-Fen Liu[10], Peadar Cremin[10], Lukas Makris[10], Li-Pen Tsao[10], Lisa M. Kopp[10], Shivaani Kummar[11]

1. University Hospital Seidman Cancer Center and Case Western Reserve University, Cleveland, OH. 2. University of Texas MD Anderson Cancer Center, Houston, TX. 3. Dana-Farber Cancer Institute, Boston, MA. 4. START Center for Cancer Research, Grand Rapids, Michigan. 5. START Center for Cancer Research, Salt Lake City, Utah. 6.NEXT Oncology, San Antonio, TX. 7. Sarah Cannon Research Institute, Nashville, TN. 8. Comprehensive Cancer Centers of Nevada. 9. Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL. 10. Circle Pharma, Inc. South San Francisco, CA. 11. Knight Cancer Institute, Oregon Heath & Science University, Portland, OR

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Disclosure Information

Advisory boards

- Abbvie
- Amgen
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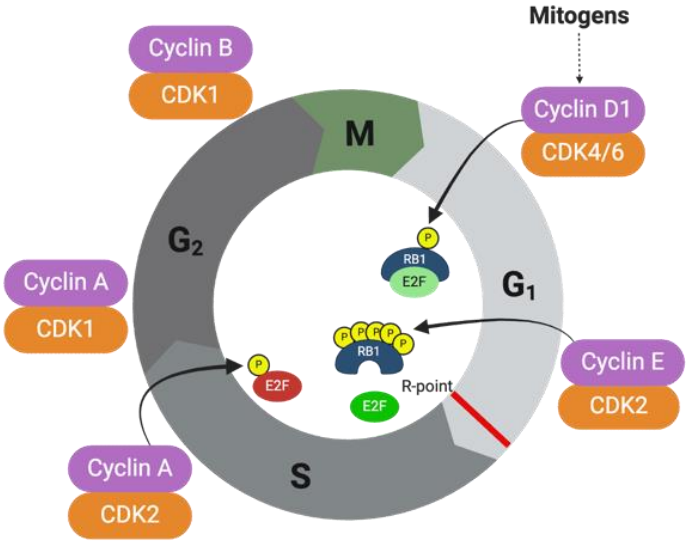
- Pfizer
- Zai Labs

CDK-Rb-E2F axis is a molecular checkpoint critical for tumor suppression

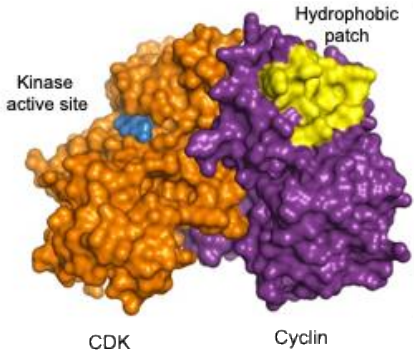


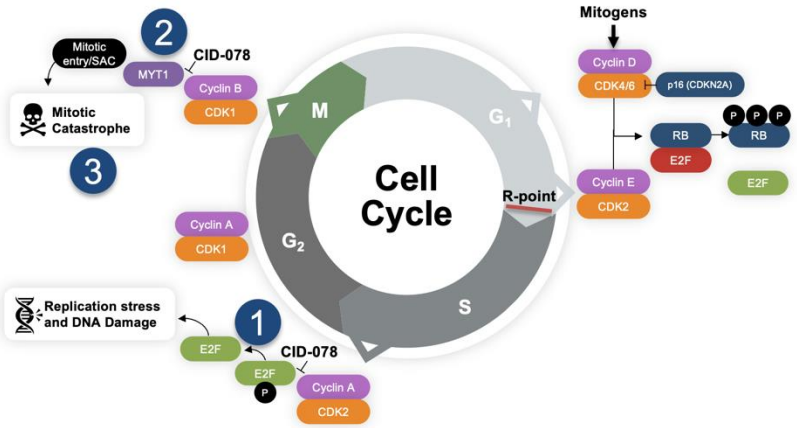
- The CDK-Rb-E2F axis regulates cell-cycle progression, with Rb acting as a molecular break silencing E2F-target genes required for S, G2- and M-phases of the cell-cycle[1-3].
  - Alterations in CDKs, cyclins, and Rb protein function can increase oncogenic E2F activity, leading to uncontrolled proliferation.
- Loss of *RB1* occurs in ≈7% of all solid tumors[4].
  - > 90% of SCLC[5]
  - > 80% of leiomyosarcoma[6]
  - Up to 70% of basal-like breast cancer, including TNBC[2]
  - Up to 70% of neuroendocrine carcinoma[7]
  - Up to 60% of osteosarcoma[8]

CDK, cyclin-dependent kinase; *RB1*, retinoblastoma transcriptional corepressor 1; SCLC, small cell lung cancer; TNBC, triple-negative breast cancer.

1. Venkadakrishnan et al., *Mol Cancer Res.* 2023;21:497–510. 2.Mandigo et al., *Clin Cancer Res.* 2022;28:255–64. 3. Chinnam and Goodrich., *Curr Top Dev Biol.* 2011;94:129–169. 4. Incidence from ACS Facts and Figures, 2025. 5. Febres-Aldana et al., *Clin. Cancer Res.* 2022; 28(21):4702-4713. 6. Cope et al., *Cancers.* 2023; 15(7), 2099. 7. Beltran et al., *Nat Med.* 2016; 22(3):298-305. 8. Zoumpoulidou et al., Nature Comms., 2016 ;12(1):7064.

CID-078 is a first-in class cyclin A/B RxL inhibitor[1]





- CID-078 is a novel, first-in-class, oral macrocycle that binds previously undruggable hydrophobic patch on cyclin A & cyclin B complexes.
  - Blocks cyclin A: E2F interaction to cause replication stress, and accumulation of DNA damage.
  - Disrupts cyclin B: Myt1 interaction forces-tumor cells into mitosis, leading to activation of the spindle assembly checkpoint (SAC).
  - The combined dual-action leads to mitotic catastrophe and apoptosis.

1. Singh S et al, *Nature*. 2025; 646, pages 734–745.

CID-078 anti-proliferative effect observed in solid tumor preclinical models

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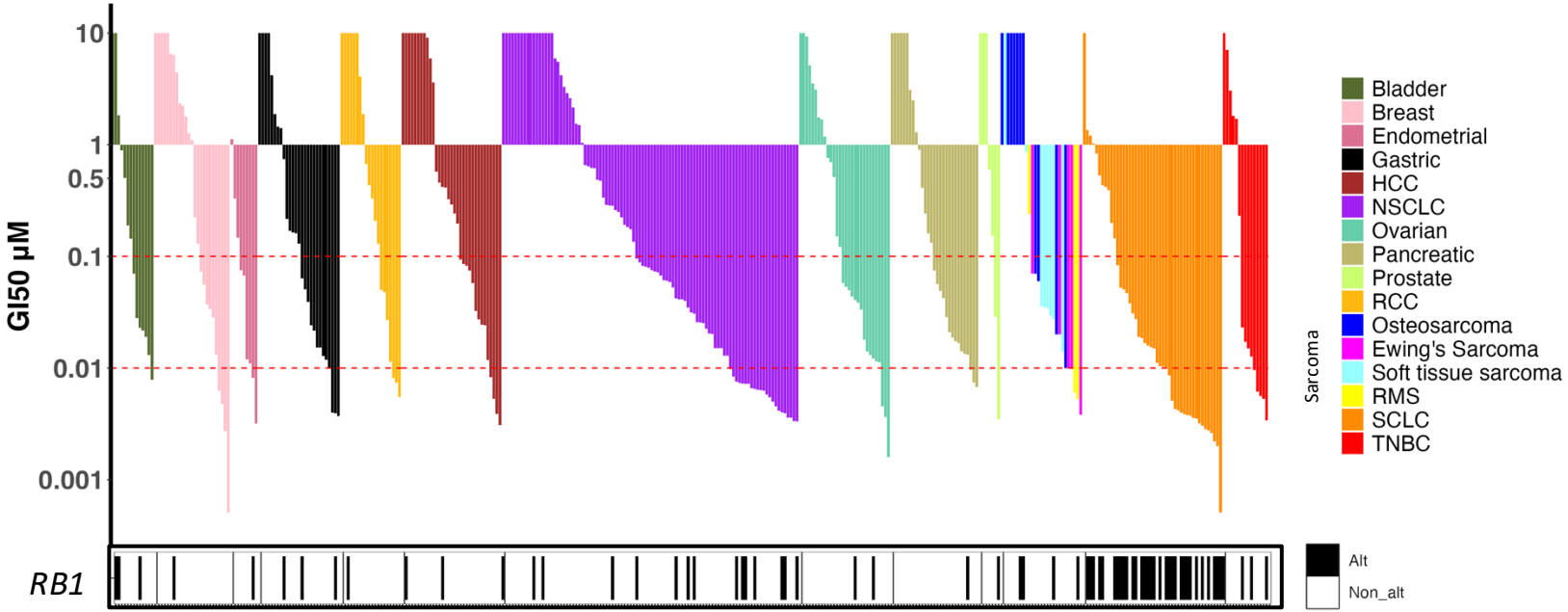
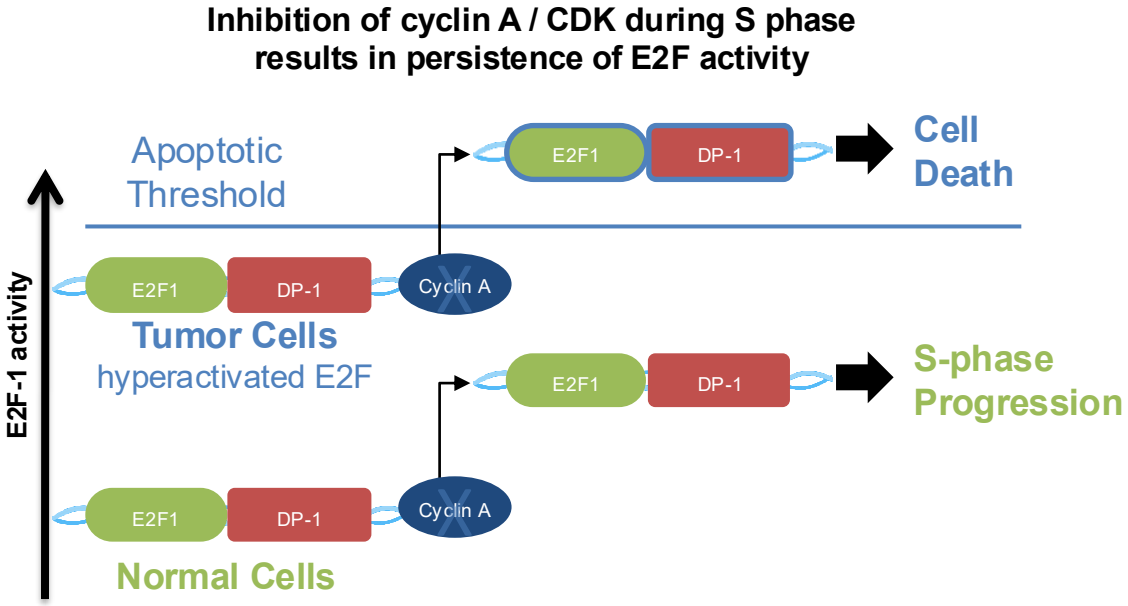


HCC, hepatocellular carcinoma; NSCLC, non-small cell lung cancer; *RB1*, retinoblastoma transcriptional corepressor 1; RCC, renal cell carcinoma; RMS, rhabdomyosarcoma; SCLC, small cell lung cancer; TNBC, triple-negative breast cancer.

Crossing the E2F activity threshold (“tipping point”) during S-phase induces apoptosis

Tumors with hyperactivated E2F susceptible to potential cell death through cyclin A inhibition



- Persistence of E2F during S-phase results in different outcomes based on baseline:
  - Normal cells: Tolerable, and cells progress normally through the cycle.
  - E2F high tumors: Crosses E2F activity threshold (“tipping point”), inducing apoptosis.

Schematic adapted from Shapiro, Journal of Clinical Oncology (2006).

CID-AB1-24001: First-in-human Phase 1 trial evaluating CID078 in solid tumors (NCT06577987)

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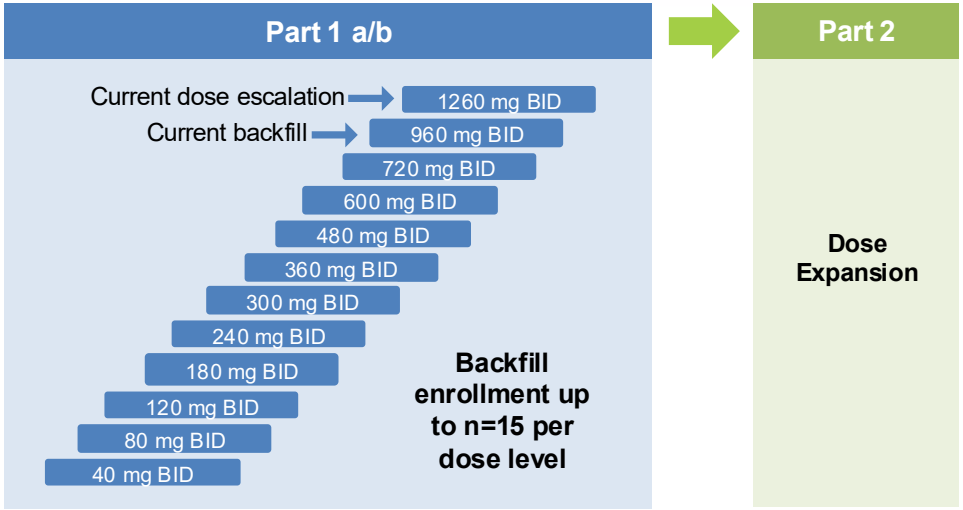

- Open-label, multicenter study to evaluate CID-078 in patients with advanced solid tumor malignancies.
- CID-078 administered orally, BID in 21-day cycles until disease progression, unacceptable safety concerns or patient withdrawal.
- Dose escalation guided by BF-BOIN design, with up to 15 patients enrolled per dose level
- Patients with SCLC, TNBC, solid tumors with *RB1*-alteration or *CDKNA2A/B* deletion eligible for backfill.
- Evaluation of increased drug loading (Gen-2) CID-078 formulation and food effect.

Primary objectives (Part 1a/b)

- Evaluate the safety and tolerability of CID-078.
- Determine the CID-078 RDE to be examined in Dose Expansion.

Selected secondary objectives (Part 1a/b)

- Evaluate tumor response/clinical activity of CID-078.
- Characterize the PK of CID-078.
- Investigate the PK exposure between the original and Gen-2 CID-078 formulations (Part 1b).
- Evaluate the effect of food on the PK of CID-078.

Key exploratory objectives (Part 1a/b)

- Blood and tumor biomarkers.
- PK/pharmacodynamic correlations with safety and efficacy endpoints.

BF-BOIN, backfill-bayesian optimal internal design; Gen, generation; PK, Pharmacokinetics; *RB1*, retinoblastoma transcriptional corepressor 1; RDE, recommended dose for expansion; SCLC, small cell lung cancer; TNBC, triple-negative breast cancer.

CID-AB1-24001: Patient demographics and disease characteristics

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Characteristics	Patients (N=79)
Age, median (range) in years	62 (27-82)
Sex, n (%)	
Male	33 (41.8)
Female	46 (58.2)
Race	
White	52 (65.8)
Black/African American	9 (11.4)
Asian	9 (11.4)
American Indian/Alaska Native	1 (1.3)
Other	8 (10.1)
Ethnicity, n (%)	
Hispanic/Latino	6 (7.6)
Not Hispanic/Latino	71 (89.9)
Not reported	1 (1.3)
Unknown	1 (1.3)
ECOG status, n (%)	
1	27 (34.2)
0	52 (65.8)

Characteristics	Patients (N=79)
Tumor type, n (%)	
Sarcoma*	19 (24.1)
Squamous cell carcinoma	10 (12.7)
SCLC	9 (11.4)
TNBC	8 (8.9)
HER2 negative breast cancer	4 (5.1)
NSCLC	4 (5.1)
Neuroendocrine	3 (3.8)
GI cancers**	12 (15.2)
Other	10 (12.7)
Prior lines of systemic therapy	
Median (range)	3 (1−11)
1L, n (%)	7 (8.9)
2L, n (%)	21 (26.6)
≥ 3L, n (%)	51 (64.5)
Biomarkers, n (%)	
RB1 alteration	45 (57.0)
CDKN2A/B loss	11 (13.9)
RB1 & *CDKN2A/B* loss	2 (2.5)

As of March 5th, 2026. Percentages may not add up to 100 due to rounding. NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; TNBC, triple-negative breast cancer.
* Includes 17 soft-tissue sarcoma (including 9 leiomyosarcomas) and 2 chondrosarcomas
** Includes 5 pancreatic cancer, 3 colorectal cancer, 2 cholangiocarcinoma, 1 esophageal and 1 gastroesophageal junction adenocarcinoma

CID-AB1-24001: Safety profile (TEAE >5% all grades)

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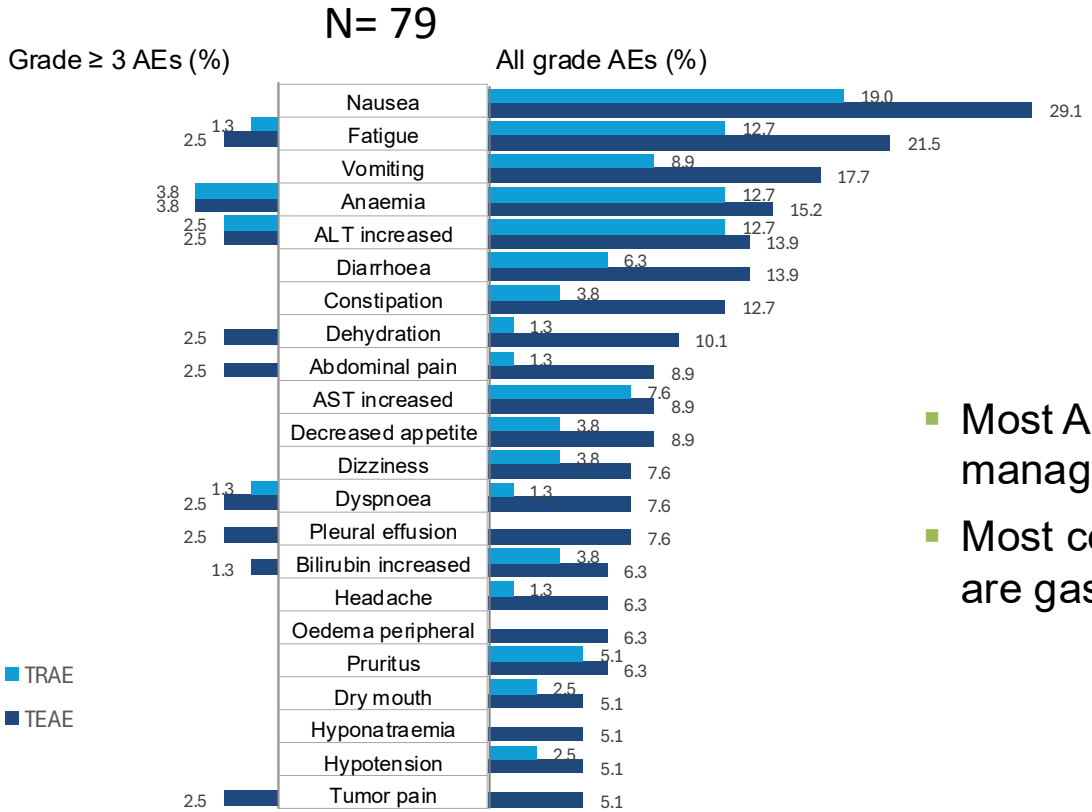

- Most AEs were grade 1 or 2 and manageable.
- Most commonly reported TEAEs are gastrointestinal in nature.

As of March 5th, 2026. AE, adverse events; TE, treatment-emergent; TR, treatment-related.

CID-AB1-24001: Safety profile is consistent, irrespective of dosing assignment

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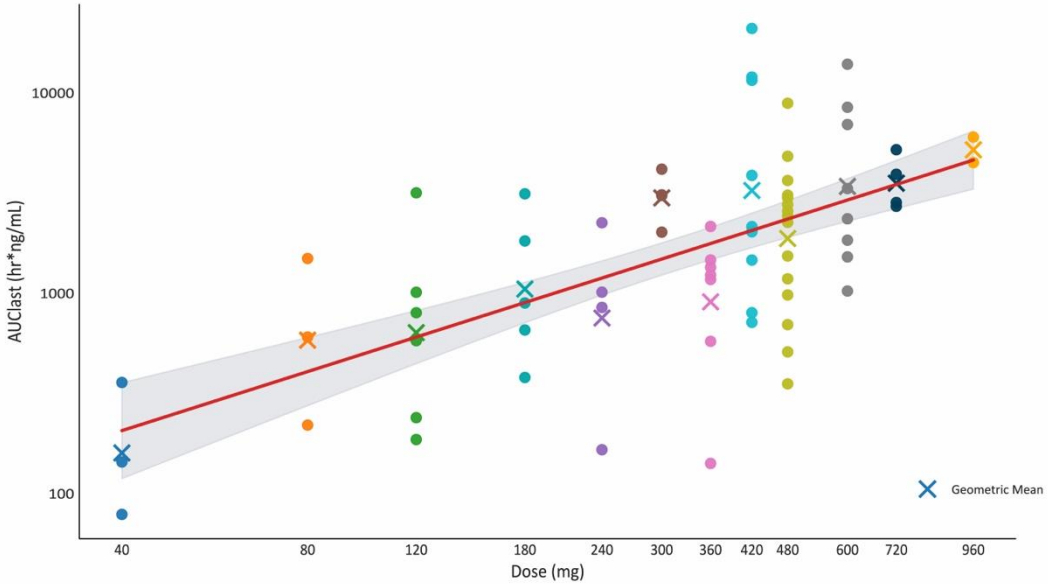
AE category	Total N=79 n (%)	40-300 mg N=28 n (%)	360 mg N=8 n (%)	420 mg N=10 n (%)	480 mg N=18 n (%)	600 mg N=10 n (%)	720 mg N=5 n (%)
Any AE	73 (92.4)	28 (100)	8 (100)	8 (80.0)	17 (94.4)	9 (90.0)	3 (60.0)
TRAE all grades	52 (65.8)	21 (75.0)	6 (75.0)	7 (70.0)	11 (61.1)	6 (60.0)	1 (20.0)
TEAE ≥ grade 3	27 (34.2)	9 (32.1)	3 (37.5)	6 (60.0)	5 (27.8)	4 (40.0)	-
TRAE ≥ grade 3	7 (8.9)	2 (7.1)	-	3 (30.0)	1 (5.6)	1 (10.0)	-
TEAE with outcome of death	1 (1.3)	1 (3.6)	-	-	-	-	-
TRAE with outcome of death	-	-	-	-	-	-	-
TEAE leading to treatment discontinuation	5 (6.3)	2 (7.1)	-	2 (20.0)	1 (5.6)	-	-
TRAE leading to treatment discontinuation	1 (1.3)	1 (3.6)	-	-	-	-	-
AEs resulting in dose modification	22 (27.8)	8 (28.6)	3 (37.5)	4 (40.0)	2 (11.1)	5 (50.0)	-
Dose interruption	22 (27.8)	8 (28.6)	3 (37.5)	4 (40.0)	2 (11.1)	5 (50.0)	-
Dose reduction	3 (3.8)	1 (3.6)	-	-	1 (5.6)	1 (10.0)	-
SAE	18 (22.8)	6 (21.4)	3 (37.5)	5 (50.0)	2 (11.1)	2 (20.0)	-
SAEs related to study drug	-	-	-	-	-	-	-

- Safety data to date suggests no apparent dose-safety relationship.
- Two dose-limiting toxicities reported with neither limiting subsequent dose escalation.
  - Grade 3 ALT increase and grade 4 GGT increase in 1 patient (300 mg BID backfill cohort) resulting in a brief drug hold; recurred at a lower dose leading to study drug discontinuation.
  - Grade 3 ALT increase in 1 patient (600 mg BID cohort), which resolved on a brief drug hold; subsequently treated at a lower dose without recurrence.
  - No associated bilirubin increase reported in either patient.

As of March 5th, 2026.
AE, adverse event; ALT, alanine aminotransferase; GGT, Gamma-glutamyl transferase; SAE, serious AE; TE, treatment-emergent; TR, treatment-related.

CID-AB1-24001: Pharmacokinetics of CID-078, a 1000Mwt macrocyclic peptide

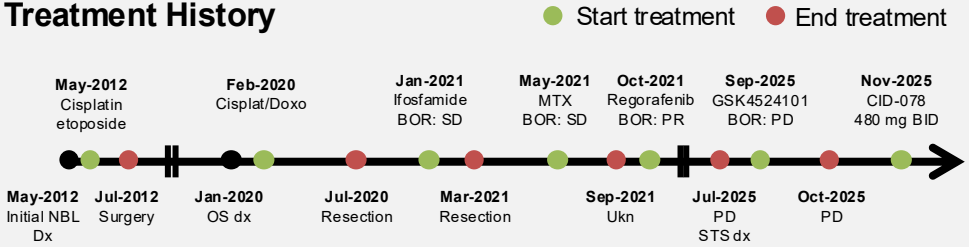


- Linear PK across dose range 40 mg to 960 mg.
- Clinical exposures consistent with preclinical predictions of human oral bioavailability ≈ 19%.
- Mean $t_{1/2}$ range ≈ 3 hours.
- No accumulation of CID-078 observed.
- No evidence of exposure saturation.

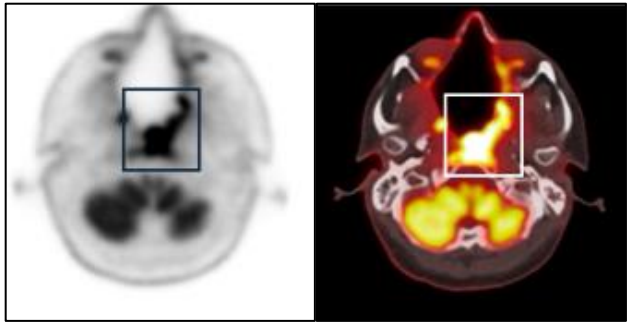
CID-AB1-24001: Patient with stage 4 *RB1*-alt undifferentiated pleomorphic sarcoma

- 28-year-old male with Li-Fraumeni Syndrome with stage IV, undifferentiated pleomorphic sarcoma; prior cancer history include esthesioneuroblastoma, diagnosed in 2012 and radiation-associated osteosarcoma diagnosed in 2020.
- Six prior lines of systemic therapy.
- CGP showed Rb K65Rfs*12 loss of function (VAF 70.3%), TP53 germline c.404G>A.

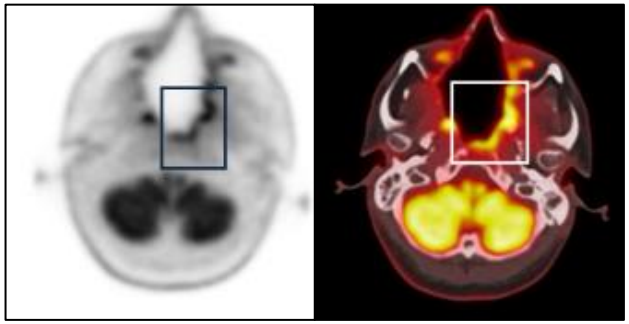
Treatment History

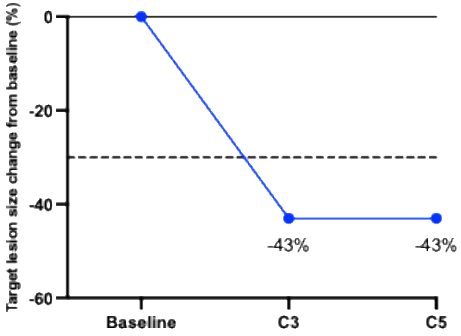


Baseline



Cycle 3, day 1



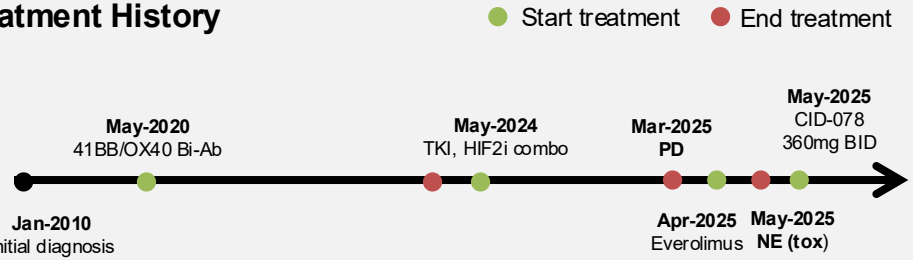


As of March 5th, 2026. Images courtesy, Dr. Yap, MD Anderson Cancer Center, Houston, TX
C, cycle; CGP, comprehensive genomic profile; NBL, neuroblastoma; VAF, variant allele frequency.

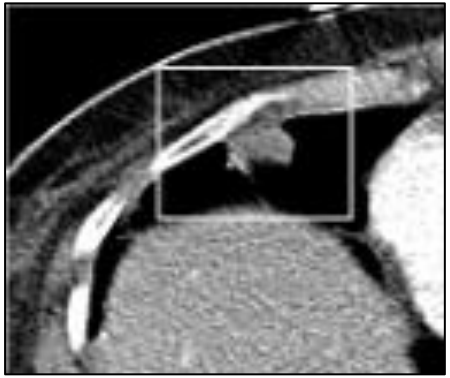
CID-AB1-24001: Patient with stage 4 well-differentiated low-grade neuroendocrine tumor

- 74-year-old female with stage IV, neuroendocrine tumor in duodenum with liver disease involvement.
- Three prior lines of therapy since initial diagnosis in 2010.
- Immunoperoxidase stain positive for CDX2, CK19 and synaptophysin, negative for CK7, CK20, GATA3, Estrogen (ER <1%) and Ki67 index <1% (low).
- Rb protein loss identified by IHC after enrollment.

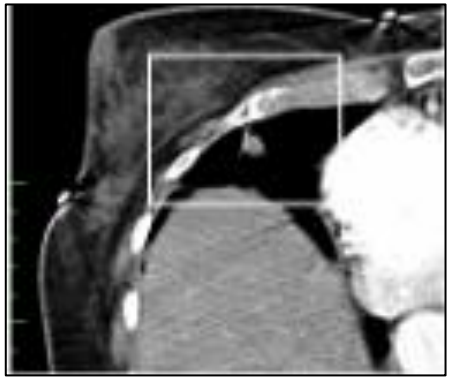
Treatment History

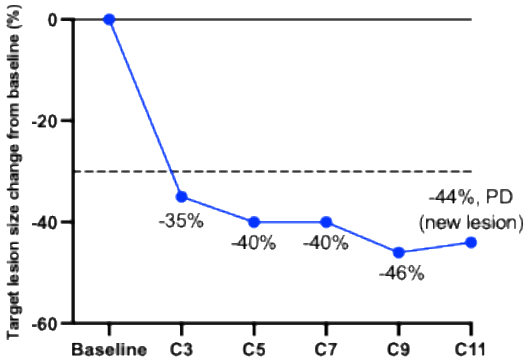


Baseline



Cycle 5, day 1





As of March 5th, 2026. Images courtesy, Drs. Subbaiah and Bhamidipati, Sarah Cannon Research Institute, Nashville, TN

Conclusions

- Novel oral macrocycle dual cyclin A/B RxL inhibitor.
- PK analysis shows linear increases in exposure with dose.
- Favorable safety and tolerability profile through highest dose tested as of cut date (720mg BID).
  - Dose limiting toxicity of ALT increase reported in 1 patient at 300 mg BID and 1 patient at 600 mg BID.
  - TRAEs ≥ Gr. 3 observed in 7 (8.9%) patients w/ 1 discontinuation due to TRAE at 300mg BID.
- Hypothesis that *RB1* loss / E2F high tumors will be sensitive to dual-inhibition of cyclin A/B is being evaluated.
  - Encouraging early signs of anti-tumor activity observed.
- Planning to evaluate "*RB1*-driven/E2F high" tumor types, such as sarcoma, neuroendocrine carcinoma (including SCLC), TNBC, and others, in expansion cohorts.

Acknowledgements

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  - University Hospital Seidman Cancer Center and Case Western Reserve University, Cleveland, OH.
  - University of Texas MD Anderson Cancer Center, Houston, TX.
  - Dana-Farber Cancer Institute, Boston, MA.
  - START Center for Cancer Research, Grand Rapids, Michigan.
  - START Center for Cancer Research, Salt Lake City, Utah.
  - NEXT Oncology, San Antonio, TX.
  - Sarah Cannon Research Institute, Nashville, TN.
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  - Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL.
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