A Dose-Escalation and Safety Study of CID-103 Followed by a Randomized, Open-label, Parallel-Arm Multi-Dose Study Evaluating the Efficacy and Tolerability of CID-103 in Adults with Persistent or Chronic Immune Thrombocytopenia

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INTRODUCTION

ITP is an autoimmune disorder characterized by a decreased platelet count due to accelerated destruction and impaired production of platelets. Anti-CD38 antibodies reduce pathological autoantibodies by depleting plasma cells, deplete other effector cells such as NK cells, and have been demonstrated to be active in treating autoimmune diseases.

CID-103, a novel anti-CD38 antibody, recognizes a unique epitope on the CD38 glycoprotein. This molecule was selected for higher antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and decreased complement-dependent cytotoxicity (CDC).

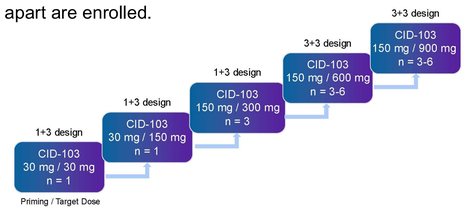
We report preliminary safety, pharmacodynamics (PD), PK, and efficacy results of a Phase 1 study of CID-103 in patients with chronic ITP conducted in China (NCT07017725). The IND / CTA were approved by FDA and Chinese CDE.

OBJECTIVES

- Primary safety endpoint is to evaluate dose-limiting toxicities (DLT) and treatment-emergent adverse events (TEAEs) related to CID-103.
- Primary efficacy endpoint is the proportion of patients achieving a platelet response, which was defined as a platelet count ≥ 50 x 10^9/L and ≥ 20 x 10^9/L above baseline on at least 2 consecutive measurements at least 7 days apart. Other standard efficacy endpoints were evaluated.
- Evaluation of PK and PD markers.

METHODS

- Open-label, dose-escalating Phase 1 study in adults with primary ITP who have received at least two previous lines of treatments and whose mean platelet count is ≤ 35 x 10^9/L on at least two measurements at least one week apart are enrolled.



- Protocol incorporates multiple adaptive design elements such as intra-patient dose escalation, dose expansion, etc.
- CID-103 is administered QW for 5 weeks after the 1st week priming dose, and then Q2W for 6 weeks, followed by Q4W for up to 6 months.
- Standard safety reporting was per CTC5.0, and standard safety follow-up visits were undertaken.

INTERIM RESULTS

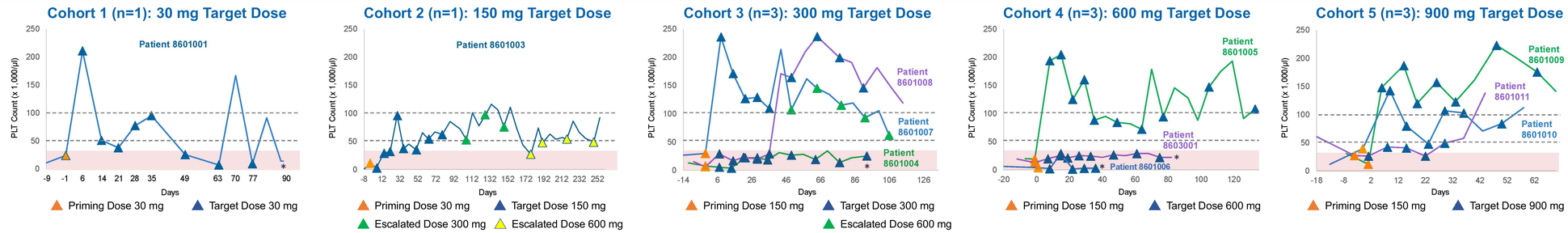
Demographic and Disease Characteristics	30 mg N=1	150 mg N=1	300 mg N=3	600 mg N=3	900 mg N=3	Total N=11
Median age, y (range)	32	29	39 (26-49)	34 (33-55)	47 (25-52)	34 (25-55)
Gender, n (%)						
Female, n (%)	1	0	1	1	2	5 (45.5%)
Male, n (%)	0	1	2	2	1	6 (54.5%)
Median duration of ITP prior to study enrollment, months (range)	14	44	27 (9-43)	89 (27-93)	14 (4-24)	27 (4-93)
Median baseline platelet count,×10^9/L (range)						
<10×10^9/L	0	0	2	1	0	3
10 to <30×10^9/L	1	1	1	2	3	8
Median # of prior ITP therapies (range)*	5	6	2 (2-3)	7 (5-10)	4 (3-4)	4 (2-10)
Karnofsky Performance Status (KPS)	100	100	100	100	100	100
Bleeding (with ITP-BAT bleeding score)						
S0M0O0	1	1	3	3	2	10
S0M0O1**	0	0	0	0	1	1
Concomitant medications, n						
Glucocorticoids	1	1	2	1	1	6
Thrombopoietin-receptor agonists	1	0	2	1	2	6

* Including Glucocorticoids, IVIg, TPO-RA, and others, ** Menorrhagia was observed in Patient 01010 in 900 mg cohort

Preliminary Safety Data	30 mg N=1	150 mg N=1	300 mg N=3	600 mg N=3	900 mg N=3	Total N=11
	n [m]*	n [m]	n [m]	n [m]	n [m]	n [m]
Any AE	1 [13]	1 [6]	3 [14]	3 [11]	3 [14]	11 [58]
DLT	0	0	0	0	0	0
Any TEAE	1 [13]	1 [6]	3 [14]	3 [11]	3 [14]	11 [58]
≥Gr 3 TEAE	1 [2]	0	0	1 [1]	1 [2]	3 [5]
Any TRAE	1 [4]	1 [3]	3 [11]	2 [5]	3 [10]	10 [33]
≥Gr 3 TRAE	1 [2]**	0	0	0	1 [2]***	2 [4]
SAE	0	0	0	0	0	0
IRR**	0	0	1 [1]	1 [1]	3 [3]	5 [5]
TEAEs leading to:						
Treatment delay	0	0	0	0	1[1]	1[1]
Dose reduction	0	0	0	0	0	0
Treatment discontinuation	0	0	0	0	0	0
Death	0	0	0	0	0	0

* n, number of patients; m, number of events
** Gr 3 anemia was reported twice on Patient 01001 but was deemed a lab error by Safety Monitoring Committee (SMC)
*** Gr 3 neutropenia and Gr 3 leukopenia were reported on Patient 01011 in Week 4 which led to a treatment delay
**** Mild IRR events, four Gr 2 (01005, 01007, 01009, and 01010) and one Gr 1 (01011), were all reported during administration of priming dose

Efficacy: Platelet Count



Platelet Count (x 1000/μL)				
ORR = 73%		Primary Endpoint: PLT ≥ 50 & ≥ 20 above baseline	Complete Response: ≥ 100	No Response
30 mg	8601001	√		
150 mg	8601003	√	√*	
300 mg	8601004			√
	8601007	√	√	
	8601008	√	√	
600 mg	8601005	√	√	
	8603001			√
	8601006			√
900 mg	8601009	√	√	
	8601010	√	√	
	8601011	√		
TOTAL	**11**	**8 / 11**	**6 / 11**	**3 / 11**

* with dose escalation

Pharmacodynamics / Pharmacokinetics

- Anti-Platelet Antibodies
  - At baseline (BL), 4 patients had detectable anti-platelet Ab (A-PA)
    - 2 patients (01005 CR, 01009 CR) reduced A-PA to non-detectable
    - 2 patients (01006 NR, 01008 CR) substantially reduced A-PA
  - 1 patient (01003) had non-detectable A-PA at BL and developed detectable A-PA after an infection assumed to be of viral origin at Day 191 (Week 28)
- % Change of plasma cell number from BL measured in 900 mg cohort
  - All 3 patients decreased from BL as follows:
    - Week 3: -52%, -82%, and -94%; Week 5: -73%, -84%, and –92%
- NK cell reduction in peripheral blood observed in all doses tested
  - Maximum reduction (~80-100%) achieved at ≥ 300 mg dose
- Reductions in IgG, IgA and IgM plateau in 300 mg cohort
- Mean receptor occupancy 58% (300 mg), 72% (600 mg), 77% (900 mg)
- $T_{1/2}$ > 60 hours (dose proportional)

SUMMARY & CONCLUSIONS

- This Phase 1 ITP study demonstrates proof-of-concept for CID-103 as a promising anti-CD38 targeted monoclonal antibody and rationale for future clinical development in diseases involving donor-directed and pathological autoantibodies
- Manageable safety profile; only two Grade 3 treatment-related events, no DLTs
- All IRRs occurred with priming dose and are due to low grade AEs
- Primary Efficacy Endpoint achieved in 8 of 11 (73%) patients
  - 6 of 8 (75%) patients achieved Complete Response (CR) with platelet improvement observed as early as one week post dose
- Reduction of PD markers (decreased anti-platelet antibodies, immunoglobulins, NK and plasma cells) is consistent with the presumed CID-103 MOA resulting in the observed platelet response
- Additional patients to be enrolled in 600 and 900 mg cohorts to expand safety / efficacy data for CID-103 in an autoimmune disease population