Application Type	BLA Resubmission after Previous Complete Response Letter
STN	125743/0/68
CBER Received Date	July 14, 2023
PDUFA Goal Date	January 12, 2024
Division / Office	DCEGM/OCE/OTP
Committee Chair	Michael Kennedy, Ph.D.
Clinical Reviewer(s)	Elizabeth Sharpe, M.D.
Project Manager	Nancy Skeeter, M.B.A.
Priority Review	No
Reviewer Name(s)	Hairong Shi, Ph.D., TEB2/DB/OBPV
Supervisory Concurrence	Yuqun Abigail Luo, Ph.D., Acting Team Lead, TEB2/DB/OBPV
	Lihan Yan, Ph.D., Branch Chief, TEB2/DB/OBPV
	John Scott, Ph.D., Division Director, DB/OBPV
Applicant	GC Biopharma Corp.
(Proposed) Trade Name	ALYGLO
Pharmacologic Class	Immune Globulin Intravenous (Human), 10% Liquid
Dosage Form(s) and Route(s) of Administration	300 – 800 mg/kg (of body weight) for intravenous infusion
Dosing Regimen	every 21 or 28 days
Indication(s) and Intended Population(s)	indicated for the treatment of primary humoral immunodeficiency in adults.

1. EXECUTIVE SUMMARY

Biologics License Application (BLA) 125743/0/68 is a resubmission for ALYGLO by GC Biopharma Corp. for a proposed indication of treatment of primary humoral immunodeficiency (PI) in adults. This resubmission includes a complete response to the Food and Drug Administration (FDA)'s Complete Response Letter (CPL) issued on February 25, 2022. The Complete Response decision was based on deficiencies in Chemistry, Manufacturing and Control (CMC). There were no deficiencies in the submitted clinical data. A statistical review memo on the original BLA submission was completed by Dr. Boris Zaslavsky; it is attached to this memo.

The efficacy database consists of data on 49 subjects treated with ALYGLO for 12 months in a single-arm study. While the treated subjects ranged in age from 3 years to 70 years and the applicant proposed the indication to be for adults (17 years of age and older) (b) (4) the clinical review team has (b) (4) . Therefore, I include in this memo the main efficacy results in adults, which were not included in Dr. Zaslavsky's statistical review memo.

The primary efficacy endpoint was annualized rate of acute serious bacterial infections (SBIs) with study success criterion defined as the upper bound of the one-sided 99% confidence interval (CI) being below 1 SBI event per person-year. Of the 33 treated adults with a total follow-up of 30.3 person-years, one acute SBI was observed. This yields an estimate of the acute SBI rate of 0.03 events per person-year with a one-sided 99% CI of (0, 0.31) events per person-year, meeting the study success criterion.

Table 1 below summarizes results for the primary and secondary efficacy endpoints.

Table 1. Summary of efficacy results

Outcome Category	Result (N=33)
Total follow-up time (person-years)	30.3
Infections	
Annualized rate of confirmed acute SBIs (events per person-year)	0.03
Annualized rate of other infections (events per person-year)	2.4
Use of therapeutic antibiotics	
Number of subjects who received intravenous (IV) antibiotics	1 (3%)
Number of days on IV antibiotics*: median (min, max)	3 (3,3)
Number of subjects who received oral antibiotics	19 (58%)
Number of days on oral antibiotics*: median (min, max)	14 (5, 63)
Missed school/work or unable to perform normal daily activities due to nfections	
Number of subjects	14 (42%)
Number of days*: median (min, max)	6 (1, 80)
Unscheduled medical visits due to infection	
Number of subjects	19 (58%)
Number of days*: median (min, max):	2 (1, 24)
Hospitalizations due to infection	
Number of subjects	2 (6%)
Number of Days*: median (min, max)	2.5 (2, 3)
Annualized rate (event days per person-year)	0.2

Note: *Statistics are based on subjects who experienced the underlying outcome.

I conclude that ALYGLO is effective in treatment of primary humoral immunodeficiency in adults and support the approval of ALYGLO.