clinical significant.

### 9.5.2 Appropriateness of Measurements

The measurements used in this in study were considered appropriate for the indication studied. Disease response is a common tool used in cancer trials to study the effectiveness of the study drug. Safety and tolerability of the study drug were reported during the trial.

### 9.5.3 Primary Efficacy Variable(s)

The primary efficacy endpoint was the Objective response rate (ORR), defined as complete response (CR) + partial response (PR), according to RECIST v1.1 criteria

### 9.5.4 Drug Concentration Measurements

Pharmacokinetic measurement was only performed on subjects enrolled in Stage I.

- PK blood samples were taken immediately pre-infusion then at 24, 25, 26, 28 and 32 hours after start of infusion on Days 1 and 8 of Cycle 3 if dose level of Cycle 3 is 24 mg/m$^2$ (time window at each sample collected: ±5 min).
- Blood samples were collected, using 10 mL sodium heparin Vacutainer® tubes. The tube was gently inverted to ensure adequate mixing of the blood sample and anticoagulant. Samples were placed on ice until separation and must be centrifuged within 20 minutes of collection. A precise record of blood sample collection times must be maintained on the appropriate source document.
- Plasma samples were analyzed via a validated high performance liquid chromatography/tandem mass spectrometry (HPLC/MS-MS) method for SCB01A.

## 9.6 DATA QUALITY ASSURANCE

The Sponsor or its designee performed the quality assurance and quality control activities of this study; however, responsibility for the accuracy, completeness, and reliability of the study data presented to the Sponsor lies with the investigator generating the data.

Audits may be conducted at the discretion of the Sponsor as part of the implementation of quality assurance to ensure that the study is being conducted in compliance with the protocol, SOPs, GCP, and all applicable regulatory requirements. Audits were independent of and separate from the routine monitoring and quality control functions. If such an audit occurred, the investigator must agree to allow access to required subject records. By signing this protocol, the Investigator granted permission to personnel from the Sponsor, its representatives, and appropriate regulatory authorities for on-site monitoring of all appropriate study documentation, as well as on-site review of the procedures employed in CRF generation, where clinically appropriate.

## 9.7 STATISTICAL METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE

### 9.7.1 Statistical and Analytical Plans

9.7.1.1 Populations for Analysis

Study subjects were categorized into the following populations for analysis:

- Intention-to-treat (ITT) population: The ITT population consisted of all subjects enrolled in the study and received at least one study treatment.

- Per-protocol (PP) population: The PP population consisted of all subjects who (1) withdrew from study for DLT, or (2) completed at least 3 cycles of study treatment regimen, have measurable baseline disease and, at least, one post-baseline RECIST assessment (PD, SD, PR or CR). Subjects with a major protocol deviation or AE, deemed by the Medical Monitor to have an impact on the study endpoints, would be excluded from the PP population.
- PK population: The PK population consisted of all subjects in stage I who received, at least, one dose of 24 $mg/m^2$ of SCB01A with sufficient post-dose bio-samples collected for PK profile characterization.

Details of any other populations for analysis were described in the statistical analysis plan (SAP).

9.7.1.2 Statistical Analysis

Both ITT and PP approaches would be included in the efficacy analyses. The efficacy conclusion would be summarized according to analyses of PP population. Safety analysis would be done on ITT population. Inferential analysis results would be expressed as point estimates and their 95% confidence intervals (CIs). Analyses would be carried out using SAS® Software, version 9.4 or higher (SAS Institute, Cary, North Carolina, USA).

All time-to-event endpoints, including OS and PFS, would be reported in days (median with 95% CI and range) and calculated using Kaplan-Meier methods. Subjects who have not progressed or who have not died at the time of the analysis would be censored at the last assessment date.

9.7.1.3 PK Evaluations

The blood samples would be assayed for SCB01A and PK parameters (maximum plasma concentration [$C_{max}$], clearance [CL], volume of distribution [$V_d$], half-life [$t_{1/2}$], elimination constant [$K_{el}$], mean residence time [MRT] and time to maximum concentration [$T_{max}$]) would be determined and presented graphically and descriptively (as appropriate).

A detailed SAP would be finalized prior to final database lock. Any significant changes to the analyses described in this protocol would be addressed in the SAP and the Clinical Study Report.

### 9.7.2 Determination of Sample Size

Assumption of sample size calculation:

- Study design: Simon's two stage design
- Type I error rate (one-sided): 5%
- Power: 80%
- Response probability of null hypothesis (P0): 0.05
- Response probability of SCB01A (P1): 0.20

According to these hypotheses, up to 37 subjects need to be recruited into the study (including 10 evaluable subjects in the Stage I and 19 evaluable subjects in Stage II, with the additional 8 subjects to account for replacement of subjects those who withdraw, i.e. dropout rate is 20%). At least 4 subjects are required to achieve CR or PR after treatment with SCB01A for the study to meet its primary objective. The trial would be discontinued if no objective response is observed after the Stage I tumor assessment review.

## 9.8 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

The statistical analysis methods have followed study protocol version 1.0, 19DEC2016, exceptions and clarifications are described below:

PK Analysis

Pharmacokinetic sampling was bio-analyzed, and PK Parameters were calculated by Protech Pharmaservices Corporation. All PK and PK parameter data were provided to Sponsor directly, no data handling, data listing nor statistical analysis on such data would be done by A2 Healthcare.

Objective response rate (ORR) definition

ORR is defined as the percentage of subjects who have achieved confirmed CR and PR during treatment phase, according to RECIST v1.1. Not-confirmed CR or PR, or withdrawn for DLT are counted as non-responder. There are 5 subjects who are not evaluated due to clinical disease progression or AE/SAE. Tumor non-evaluable subjects are tend to be treatment failure and would also be counted as non-responder (not evaluable for response), instead of counted as missing.