Study Title:	A Phase II Study of AB-16B5 combined with Docetaxel in Previously Treated Subjects with Metastatic Non-Small Cell Lung Cancer – EGIA-002 Study
NCT Number:	NCT04364620
Protocol Date	30 October 2023

Clinical Study Protocol
AB-16B5-201

Study Title:	A Phase II Study of AB-16B5 combined with Docetaxel in Previously Treated Subjects with Metastatic Non-Small Cell Lung Cancer – EGIA-002 Study
Study Number:	AB-16B5-201
Study Phase:	II
Indication:	Treatment of metastatic non-small cell lung cancer (NSCLC)
Principal Investigator:	[redacted]
Sponsor:	Alethia Biotherapeutics Inc.
Sponsor Contact:	Julie Laurin, B. Pharm., Ph.D.
[redacted]	[redacted]
Sponsor Address:	141 President-Kennedy Ave. Suite SB-5100, 5th floor Montreal, Quebec Canada H2X 1Y4

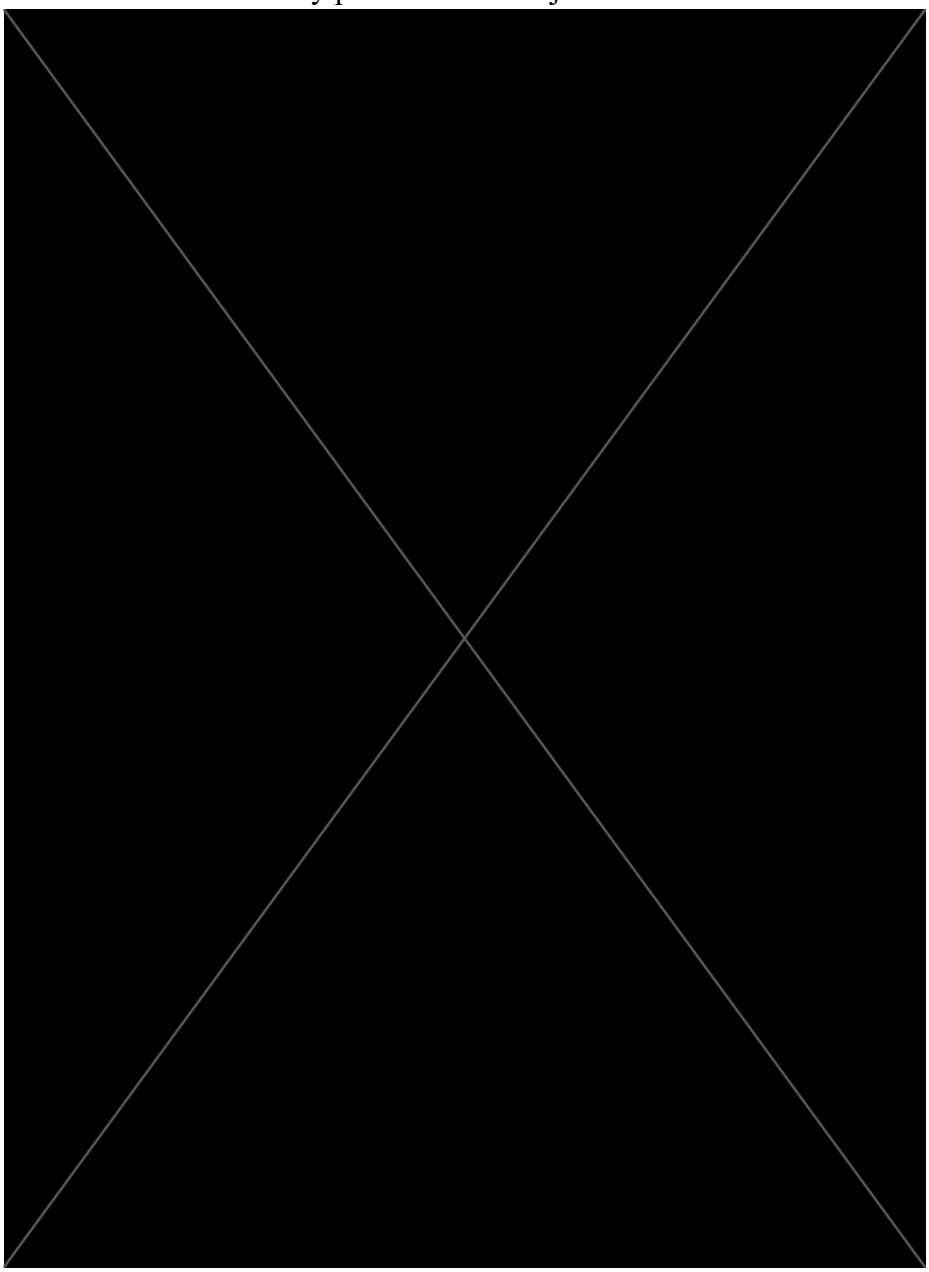
	Date
Protocol:	7 May 2020
Amendment No. 4	30 October 2023

Confidentiality Statement

SPONSOR SIGNATURE PAGE

Type of Document:	☐ Protocol ☒ Protocol amendment
Protocol Title:	A Phase II Study of AB-16B5 combined with Docetaxel in Previously Treated Subjects with Metastatic Non-Small Cell Lung Cancer
Protocol Number:	AB-16B5-201
Protocol Date:	30 October 2023

This clinical study protocol was subject to critical review and has been approved by the Sponsor.



INVESTIGATOR'S AGREEMENT

I will provide copies of the protocol, any subsequent amendments and access to all information provided by the Sponsor to the study personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the investigational study agent and the study protocol. I agree to conduct this clinical trial according to the protocol described herein, except when mutually agreed to in writing with the Sponsor. I also agree to conduct this study in compliance with Good Clinical Practice (GCP) standards as defined by the International Conference on Harmonisation (ICH) Guideline for Good Clinical Practice, all applicable national, state, and local regulations, as well as the requirements of the appropriate Research Ethics Board and any other institutional requirements.

Principal Investigator:

Signature:_____

Date:_____

PRIMARY REASONS FOR THIS AMENDMENT

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	

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1. STUDY SYNOPSIS

Study Title: A Phase II Study of AB-16B5 combined with Docetaxel in Previously Treated Subjects with Metastatic Non-Small Cell Lung Cancer – EGIA-002 Study

Abbreviated Title: AB-16B5 combined with Docetaxel in NSCLC

Study Number: AB-16B5-201

Study Phase: II

Study Period: 2020-2021

Study Design:

This is an open-label, single-arm, multi-center Phase II trial of AB-16B5 in combination with docetaxel in previously treated subjects with metastatic non-small cell lung cancer who have experienced disease progression following treatment with a platinum-containing doublet treatment and an anti-PD1 or PD-L1 immune checkpoint antibody, administered simultaneously or sequentially. Approximately 40 subjects will be enrolled in this trial and receive AB-16B5 at a dose of 12 mg/kg once weekly on Days 1, 8 and 15 combined with docetaxel at a dose of 75 mg/m^2 once every 3 weeks on Day 1. One cycle of treatment will consist of 21 days (3 weeks). The safety profile of the AB-16B5 and docetaxel combination will be examined during a safety lead-in period with the first 8 subjects completing one cycle of treatment or experiencing a DLT during Cycle 1 and being part of the DLT Evaluable population (as defined in Section 12.4.4). No dose escalation will be performed but a decision to de-escalate the AB-16B5 dose could be made using the modified toxicity probability interval method.

Radiographic imaging will be performed every 6 weeks until disease progression to assess response to treatment using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria for determination of the objective response rate (ORR) and progression free survival (PFS). Paired tumor biopsies (pre-treatment and on-treatment) will be collected in all subjects. Adverse events will be monitored throughout the study and graded for severity according to the NCI Common Terminology Criteria for Adverse Events (CTCAE). Study treatment will continue until there is evidence of disease progression (defined according to RECIST 1.1), treatment-related adverse events of unacceptable severity, subject request for discontinuation or Investigator determination that further treatment is not in the subject's best interest. Treatment through progression will be allowed if the Investigator considers the subject to be clinically stable (see Section 7.2 for definition of clinically stable).

Subjects who must discontinue AB-16B5 or docetaxel due to toxicity or any reasons other than progressive disease will continue the other treatment (AB-16B5 or docetaxel). Subjects who must discontinue both AB-16B5 and docetaxel for reasons other than progressive disease will remain in the study to obtain tumor imaging until disease progression.

A futility analysis will also be conducted with a minimum of 10 evaluable subjects (i.e., subjects who are part of the Clinical Activity Evaluable Population as defined in Section 12.4.1).

Monitoring of responses will be done every 8 subjects thereafter until up to 34 evaluable subjects are obtained or the trial is stopped for futility. The trial will be stopped for futility if either 0 confirmed response out of 10 subjects, 1 confirmed response out of 18, 2 confirmed responses out of 26 or 6 confirmed responses out of 34 are obtained. If more than 6 confirmed responses are obtained out of 34 evaluable subjects, AB-16B5 in combination with docetaxel will be considered promising.

Objectives:

Primary Objectives:

- To determine the objective response rate (ORR) per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the safety and tolerability of the combination of AB-16B5 and docetaxel

Secondary Objectives:

- To determine the clinical benefit rate (complete response (CR), partial response (PR) and stable disease (SD)) per RECIST 1.1 and the duration of clinical benefit in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the duration of response (CR and PR) per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the duration of stable disease per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the progression free survival (PFS) per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the overall survival (OS) in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the pharmacokinetics of AB-16B5 in this subject population

[redacted]

Diagnosis and Criteria for Inclusion:

Inclusion Criteria

Subjects enrolled in the study must meet the following inclusion criteria:

1. Subjects (male or non-pregnant female) must be ≥ 18 years of age on the day of signing the informed consent.
2. Subjects with a histologically or cytologically confirmed diagnosis of (Stage III-IV) non-small cell lung cancer (NSCLC) and with at least one measurable lesion defined by RECIST 1.1.
3. Subjects must have experienced a disease progression following treatment with an anti-PD1 or PD-L1 immune checkpoint antibody and a platinum-containing doublet treatment, administered simultaneously or sequentially.
4. Subjects with a targetable driver mutation in EGFR or ALK gene will be allowed on trial after failing all available targeted therapies and having experienced a disease progression following treatment with an anti-PD1 or PD-L1 immune checkpoint antibody and a platinum-containing doublet treatment, administered simultaneously or sequentially.
5. Subjects must have adequate organ and immune function as indicated in the table below

System	Laboratory Value
Hematological	
Absolute neutrophil count (ANC)	≥ 1.5 X 10^9/L (1,500 cells/mm^3)
Platelets	≥ 100 X 10^9/L (100,000 cells/mm^3)
Hemoglobin	≥ 90 g/L
Hepatic	
Total bilirubin	≤ ULN
AST (SGOT) and ALT (SGPT)	≤ 1.5 X ULN, unless secondary to liver metastases
Alkaline phosphatase	≤ 2.5 X ULN
Renal	
Creatinine clearance[a]	≥ 50 mL/min
Coagulation	
International Normalized Ratio (INR)	≤ 1.5 X ULN[b]
Creatinine clearance should be calculated using the Cockcroft-Gault Method: Formula to use when serum creatinine is expressed in mg/dL: CrCl = [(140-age) X weight (kg) X (0.85 for females only)] / (72 X serum creatinine (mg/dL)) Formula to use when serum creatinine is expressed in μmol/L: CrCl = 1.23 X [(140-age) X weight (kg) X (0.85 for females only)] / (serum creatinine (μmol/L)) [b]if subject is receiving anticoagulant therapy, then INR must be within therapeutic range.	

6. Subjects must have a tumor lesion amenable for biopsies with no contraindication for biopsy.
7. Subjects must have an Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2.
8. Subjects must have a life expectancy of at least 3 months.
9. Subjects must have recovered from the toxic effects resulting from the most recent cancer treatment to Grade 1 or less. If the subjects underwent major surgery or received radiation therapy, they must have recovered from the complications and/or toxicity.
10. Female subjects of childbearing potential must have a negative serum pregnancy test within 72 hours prior to the first dose of study treatment.
11. Subjects (both male and female) of reproductive potential must be willing to practice highly effective methods of contraception throughout the study and for up to 90 days

after the last dose of study medication. Abstinence is acceptable if this is the subject's usual lifestyle.

12. Female subjects are not considered of childbearing potential if they have a history of surgical sterility or evidence of post-menopausal status defined as any of the following:
    - ≥ 45 years of age and has not had menses for more than 2 years.
    - Amenorrhoeic for < 2 years without hysterectomy and oophorectomy and a follicle stimulating hormone (FSH) value in the postmenopausal range at screening.
    - Post hysterectomy, oophorectomy or tubal ligation. Documented hysterectomy or oophorectomy must be confirmed with medical records of the actual procedure or by ultrasound. Tubal ligation must be confirmed with medical records of the actual procedure.
13. Subjects must understand and be able and willing and likely to fully comply with the study procedures, including scheduled follow-up, and restrictions.
14. Subjects must have given written personally signed and dated informed consent to participate in the study in accordance with the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, before completing any study related procedures.

Exclusion Criteria

1) Subjects who have received prior therapy with AB-16B5.
2) Subjects who have received prior therapy with docetaxel for the treatment of NSCLC.
3) Subjects who are currently participating or has participated in a study of an investigational agent or using an investigational device within 21 days of the first dose of study treatment. The 21-day window should be calculated using the last dose of an antineoplastic investigational agent or last use of an investigational device with antineoplastic intent.
4) Subjects who have received any anti-cancer treatment within 3 weeks or radiation therapy within 2 weeks prior to receiving the first dose of study treatment or who have not recovered from adverse events to Grade 1 or less. Subjects with alopecia are eligible to participate.
5) Subjects who are expected to require any other form of systemic or localized antineoplastic therapy while on the trial. This includes maintenance therapy with another agent or radiation therapy.

6) Subjects who are receiving a dose > 10 mg/day of prednisone (or equivalent) within 7 days prior to the first dose of study treatment or any other form of immunosuppressive medication (corticosteroid pre-treatment and/or post-treatment of docetaxel is allowed).
7) Subjects who require treatment with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole). Subjects may be included if there is an alternate treatment with a weak CYP3A4 inhibitor and they are willing to change at least 7 days prior to the first dose of study treatment.
8) Subjects who have another malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin or in situ cervical cancer.
9) Subjects who have known active central nervous system metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate if they have been clinically stable for at least 2 weeks prior to the first dose of study treatment, if they have no evidence of new or enlarging brain metastases and if they are not receiving a dose > 10 mg/day of prednisone (or equivalent) within 7 days prior to the first dose of study treatment.
10) Subjects with clinically significant ECG abnormalities.
11) Subjects who have received or will receive a live vaccine within 30 days prior to the first dose of study treatment.
12) Subjects with a known history of human immunodeficiency (HIV).
13) Subjects with an active Hepatitis B or C infection.
14) Subjects with an active infection requiring antibiotic therapy.
15) Subjects with a known history of alcohol or other substance abuse within the last year.
16) Subjects with known hypersensitivity to docetaxel or drugs formulated with polysorbate 80.
17) Subjects who have a history or current evidence of any condition, therapy or laboratory abnormalities that may confound the results of the trial, interfere with the subject's participation for the full duration of the trial or if it is not in the best interest of the subject to participate in the trial.
18) Subjects with medical, social or psychosocial factors that, in the opinion of the treating Investigator, could impact the safety or compliance with study procedures.
19) Subjects who are pregnant or lactating or who are expecting to conceive or father children within the projected duration of the trial through 90 days after the last dose of AB-16B5 or the last dose of docetaxel.

Statistical Methodology:

This is a single arm Phase II study with a safety lead-in period and a futility analysis. To assess efficacy, the primary endpoint ORR will use a Predictive Probability Design (PPD)[1]. The PPD is a flexible design that allows for the possibility to stop before the end of the trial if the treatment is not efficacious enough (futility).

Safety Lead-in Period

The assumptions to be applied in establishing the mTPI[2] methodology are:

- the maximum tolerated dose (MTD) is defined to have 0.30 probability of toxicity; and
- the acceptable variance around the MTD is ± 0.05 (i.e., the region of the MTD is 25% to 35% incidence of dose limiting toxicity (DLT)).

The mTPI model will determine the number of toxicities relative to subjects enrolled in the safety lead-in before the dose de-escalation decision is made. No dose escalation will be allowed. The number of subjects with DLTs observed relative to the number of subjects treated at a specific dose determines whether dose de-escalation is needed. The treatment will be considered acceptable if no more than 3 subjects experienced a DLT during the first cycle in the first 8 subjects treated and being part of the DLT Evaluable population. De-escalation to AB-16B5 9

mg/kg will be performed if more than 3 subjects experienced a DLT in the first 8 subjects treated. The next three subjects will then be evaluated at this lower dose. If 0 or 1 subject experienced a DLT during the first cycle in these 3 subjects, the AB-16B5 9 mg/kg dose will be considered acceptable. A final de-escalation of AB-16B5 to 6 mg/kg will be performed if more than 1 subject experienced a DLT at 9 mg/kg and the safety profile will be evaluated using the same process as described above.

For these purposes, a DLT will be defined as a ≥ Grade 3 non-hematologic toxicity occurring during Cycle 1 of therapy. In addition, the following hematologic toxicities will be considered as a DLT:

- Grade ≥ 4 neutropenia or thrombocytopenia > 7 days
- Grade ≥ 3 thrombocytopenia with bleeding
- Grade ≥ 3 febrile neutropenia

Toxicities that are clearly and incontrovertibly due to disease progression or to extraneous causes will not be considered DLTs. In addition, the following non-hematologic toxicities will not be considered DLTs:

- Grade 3 arthralgia or myalgia which returns to Grade ≤ 1 within < 7 days with appropriate supportive care
- Grade 3 nausea, vomiting or diarrhea which returns to Grade ≤ 1 within < 72 hours with appropriate supportive care
- Grade 3 fatigue lasting < 7 days
- Grade 3 electrolyte abnormalities that last less than 72 hours and are not associated with clinical symptoms
- Grade 3 amylase or lipase elevation which is not associated with symptoms or clinical manifestations of pancreatitis

Statistical Analyses

The primary endpoint of ORR will be tested using PPD. Descriptive statistics including the number of evaluable subjects, the percentage of subjects, and the 95% confidence interval will be presented for ORR and clinical benefit rate. Duration of response, duration of stable disease, duration of clinical benefit, PFS and OS will be analyzed using Kaplan-Meier method to account for censoring data.

Pharmacokinetic Analyses

Noncompartmental analysis (NCA) of pharmacokinetic data will be conducted using standard approaches which will be defined in a separate analysis plan. If feasible, the peak concentration (C_{max}), area under the concentration time curve (AUC), clearance (CL), volume of distribution (Vz) and half-life will be reported. Summary statistics will be provided.

The pharmacokinetic data may also be evaluated using a population pharmacokinetics approach.

2. LIST OF ABREVIATIONS

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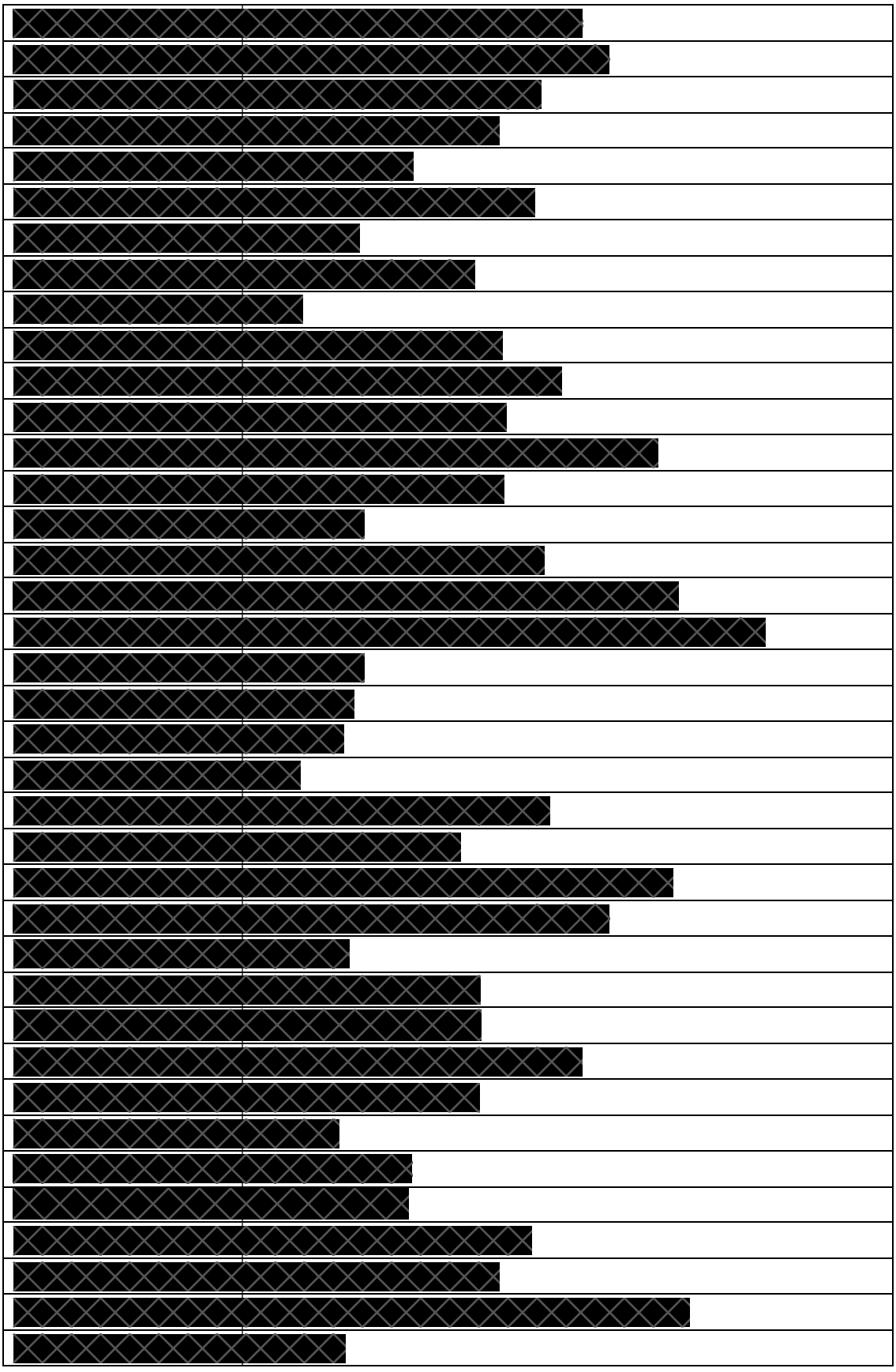

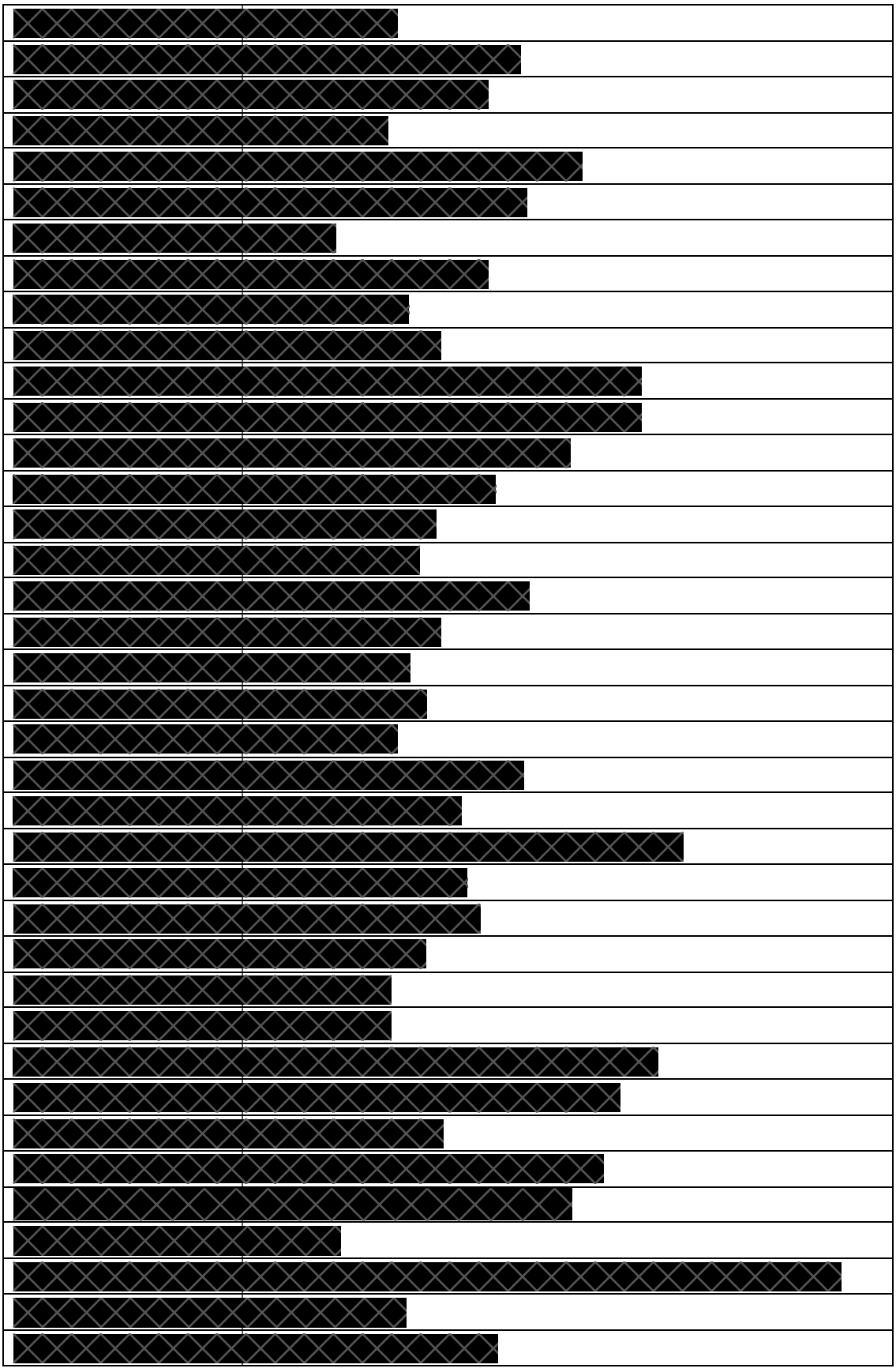

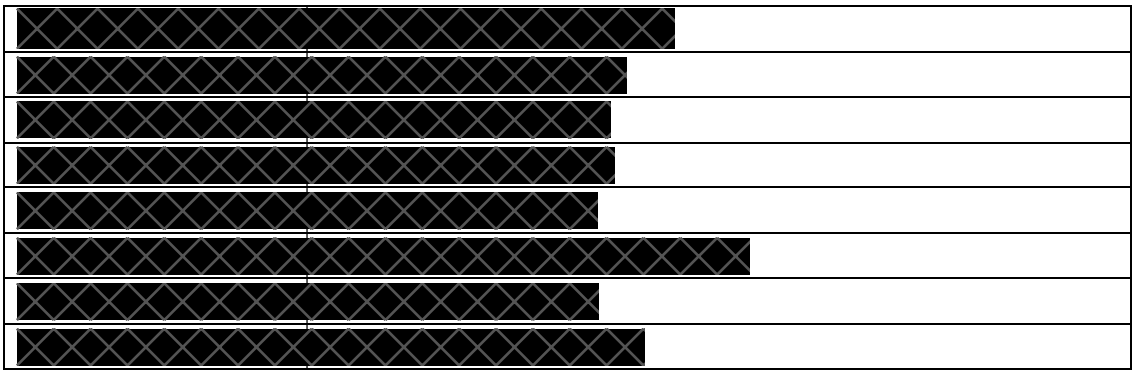

3. INTRODUCTION

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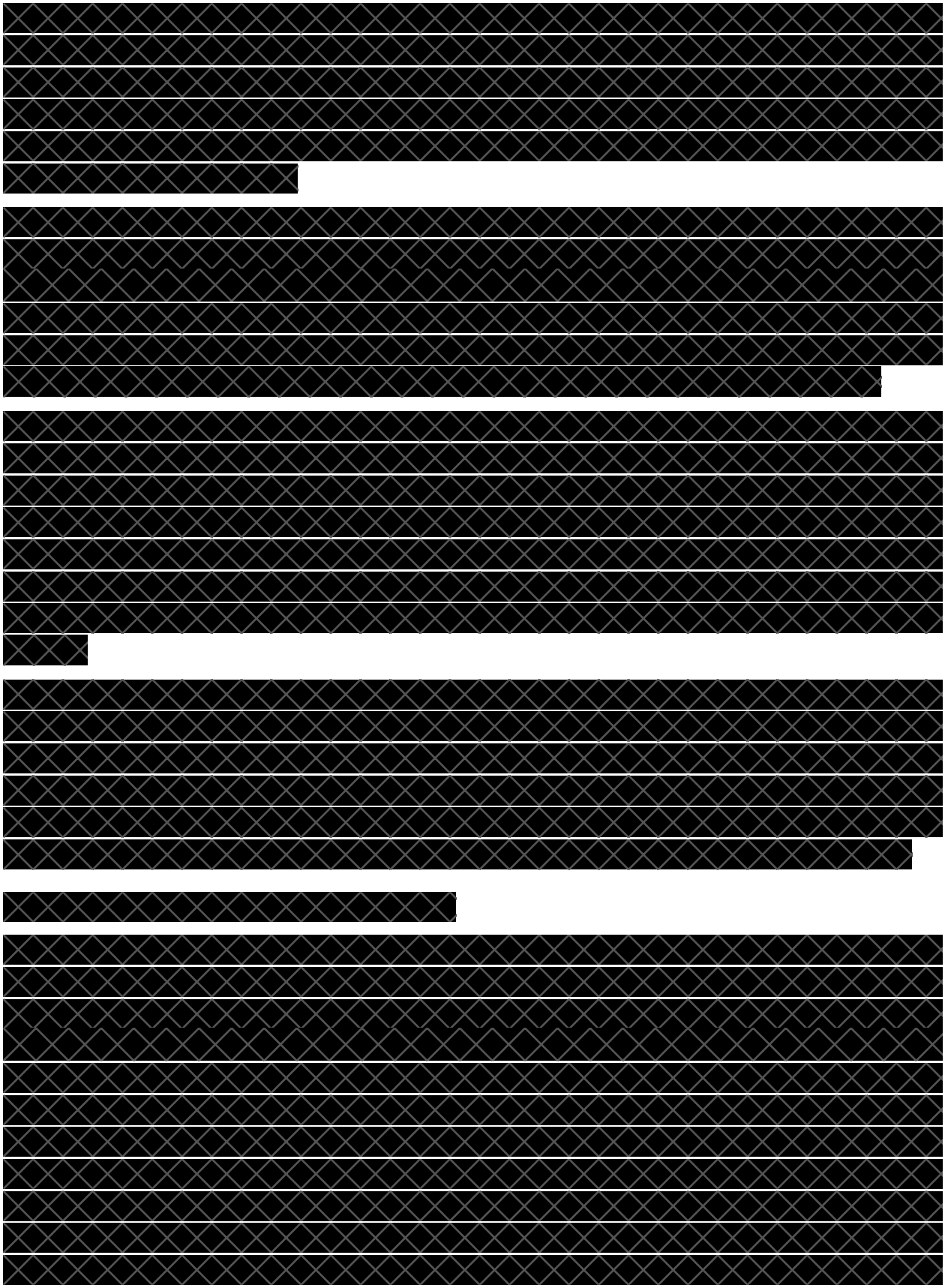

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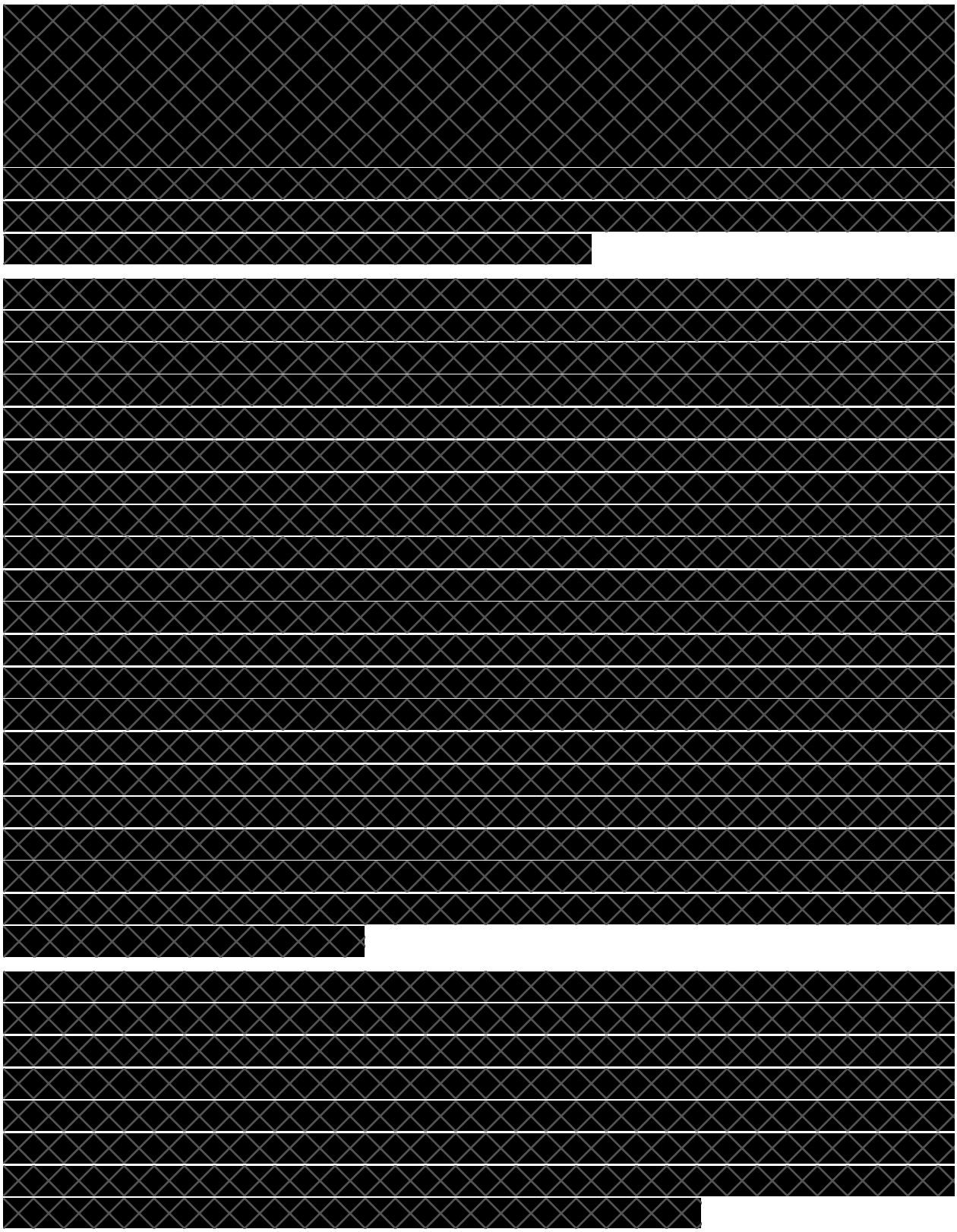

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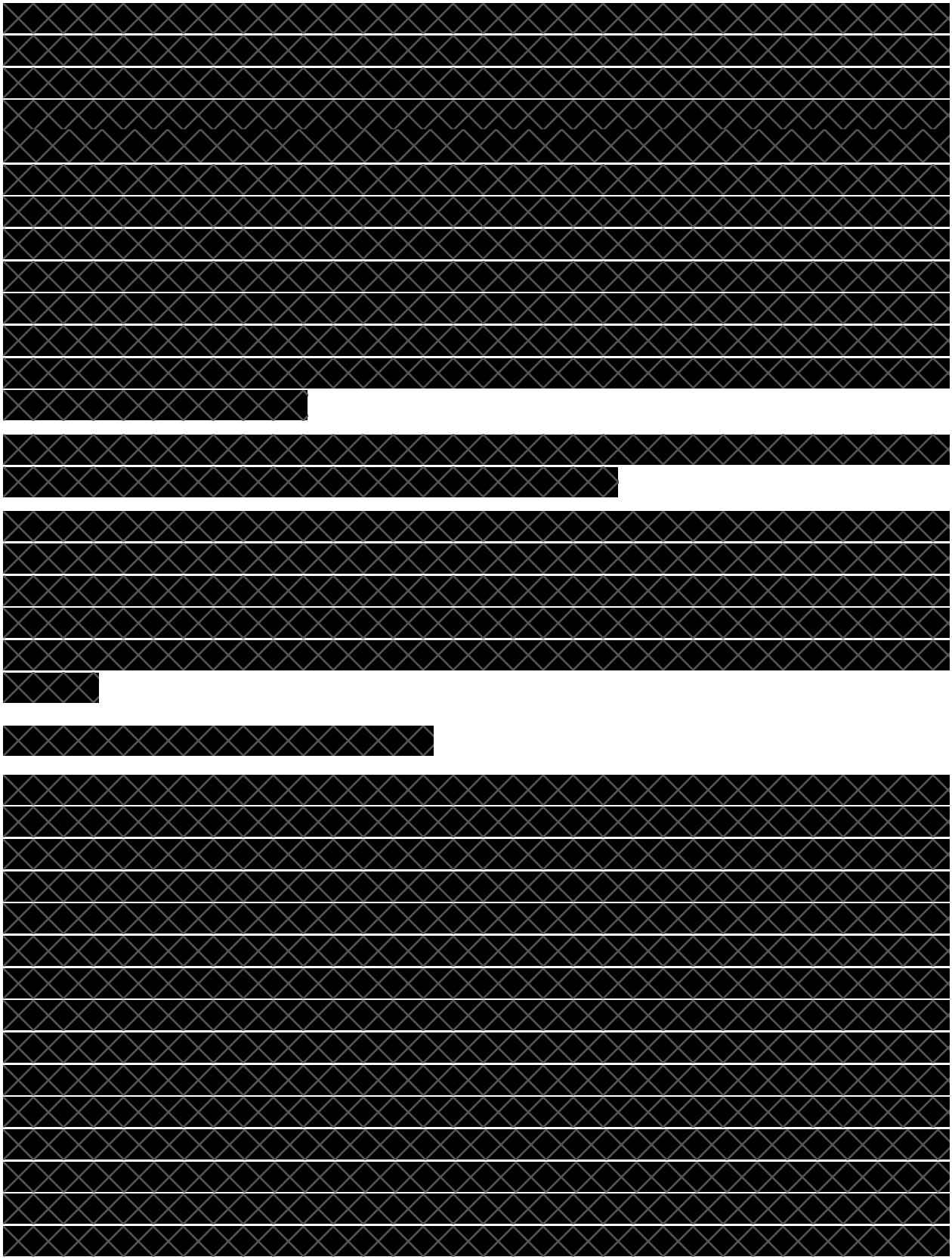

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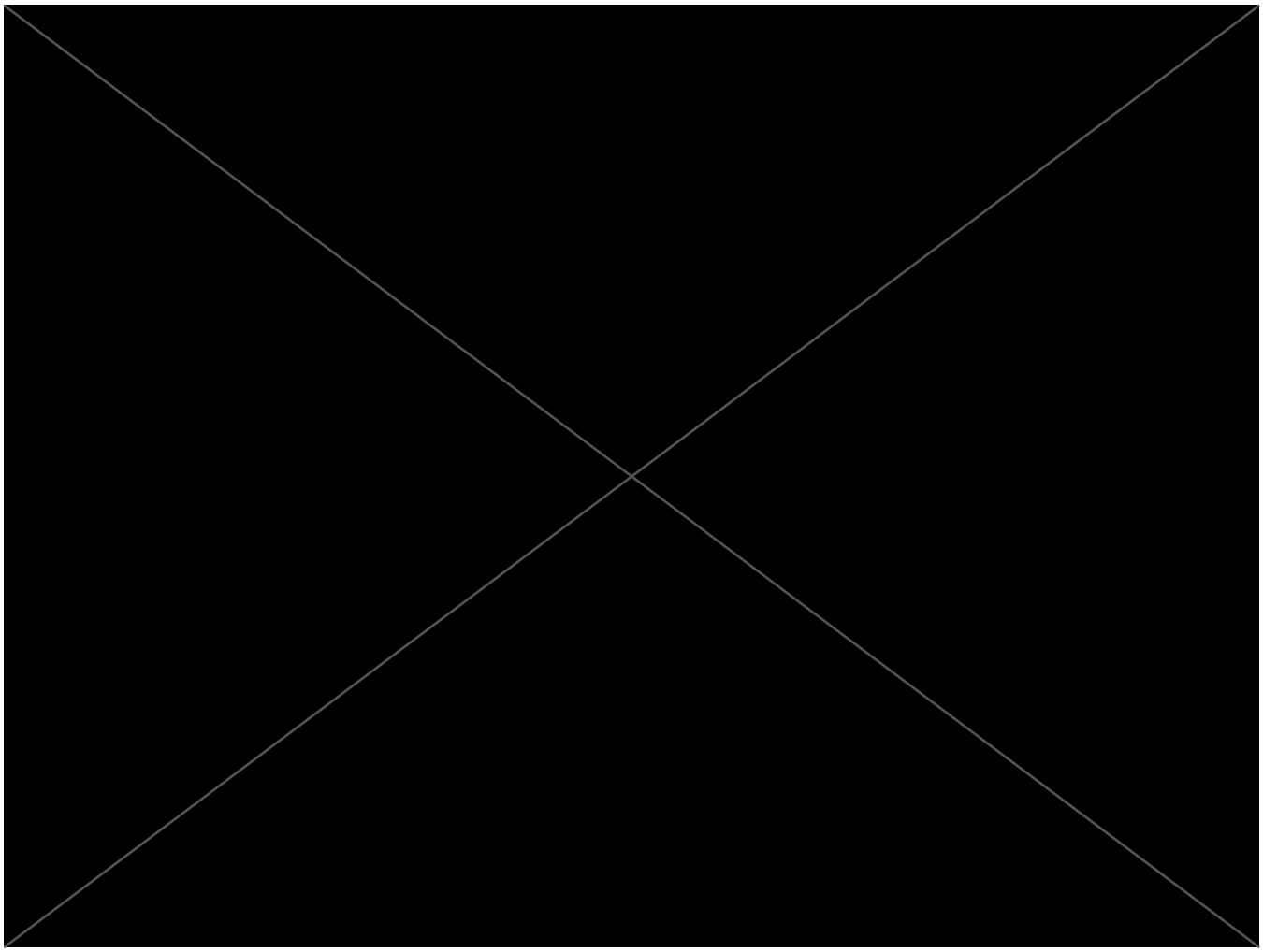

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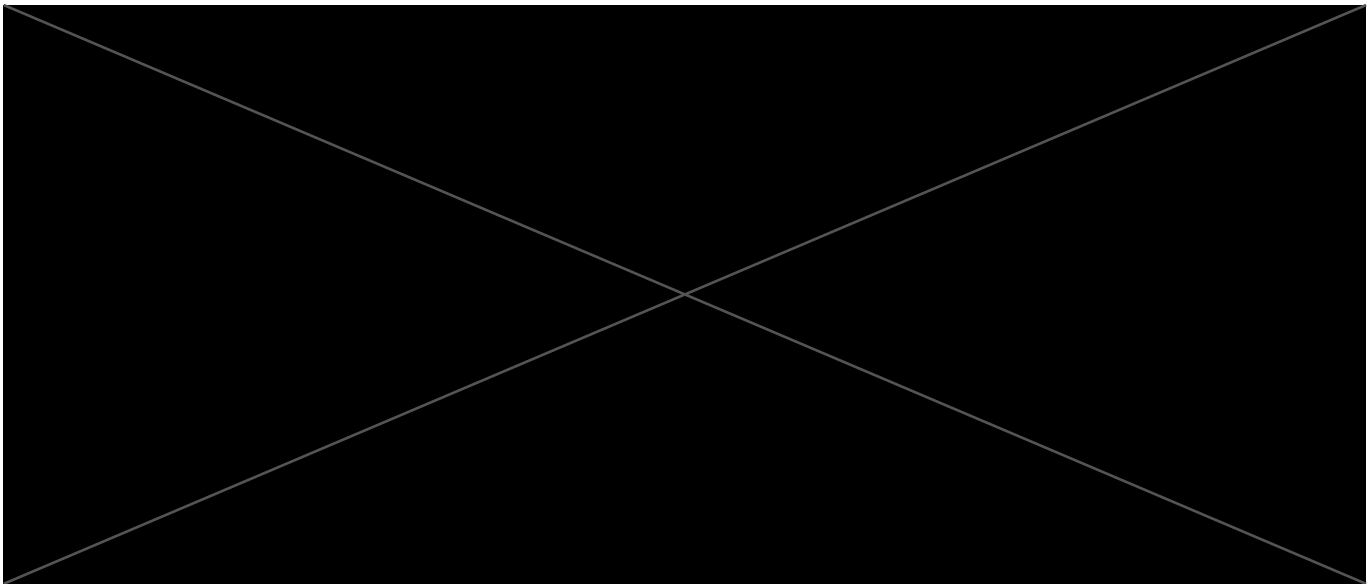

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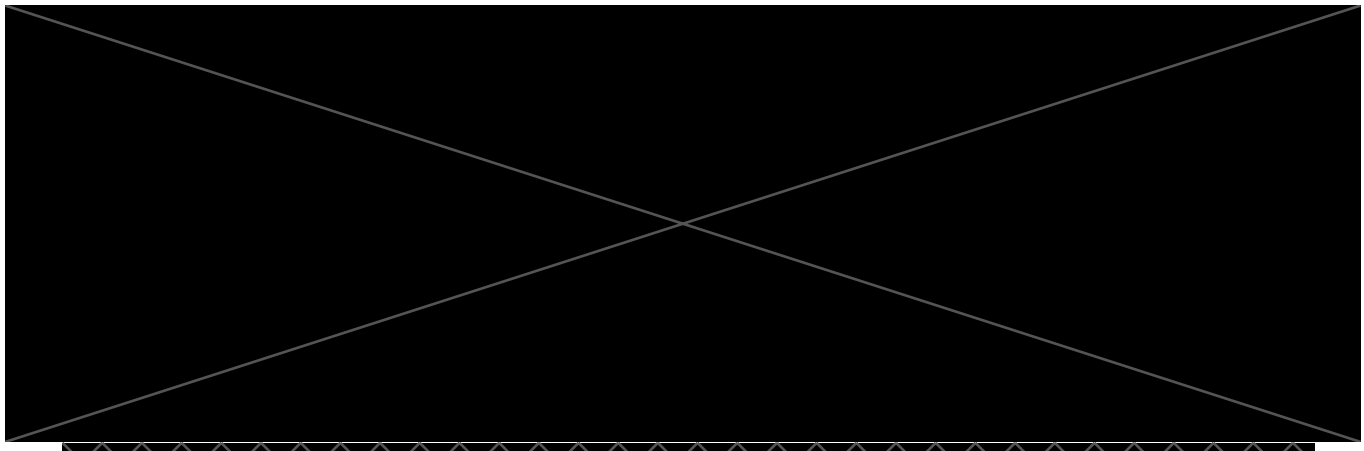
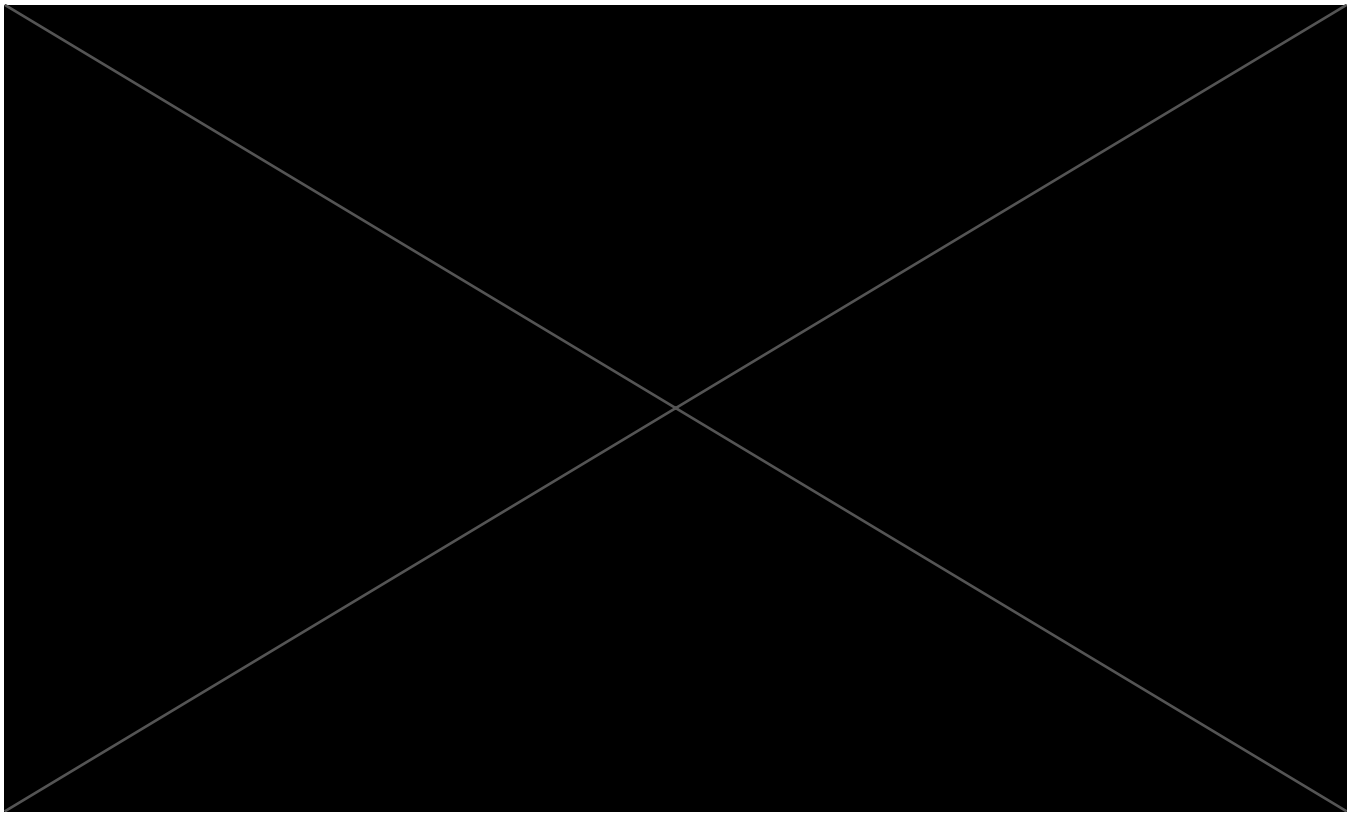
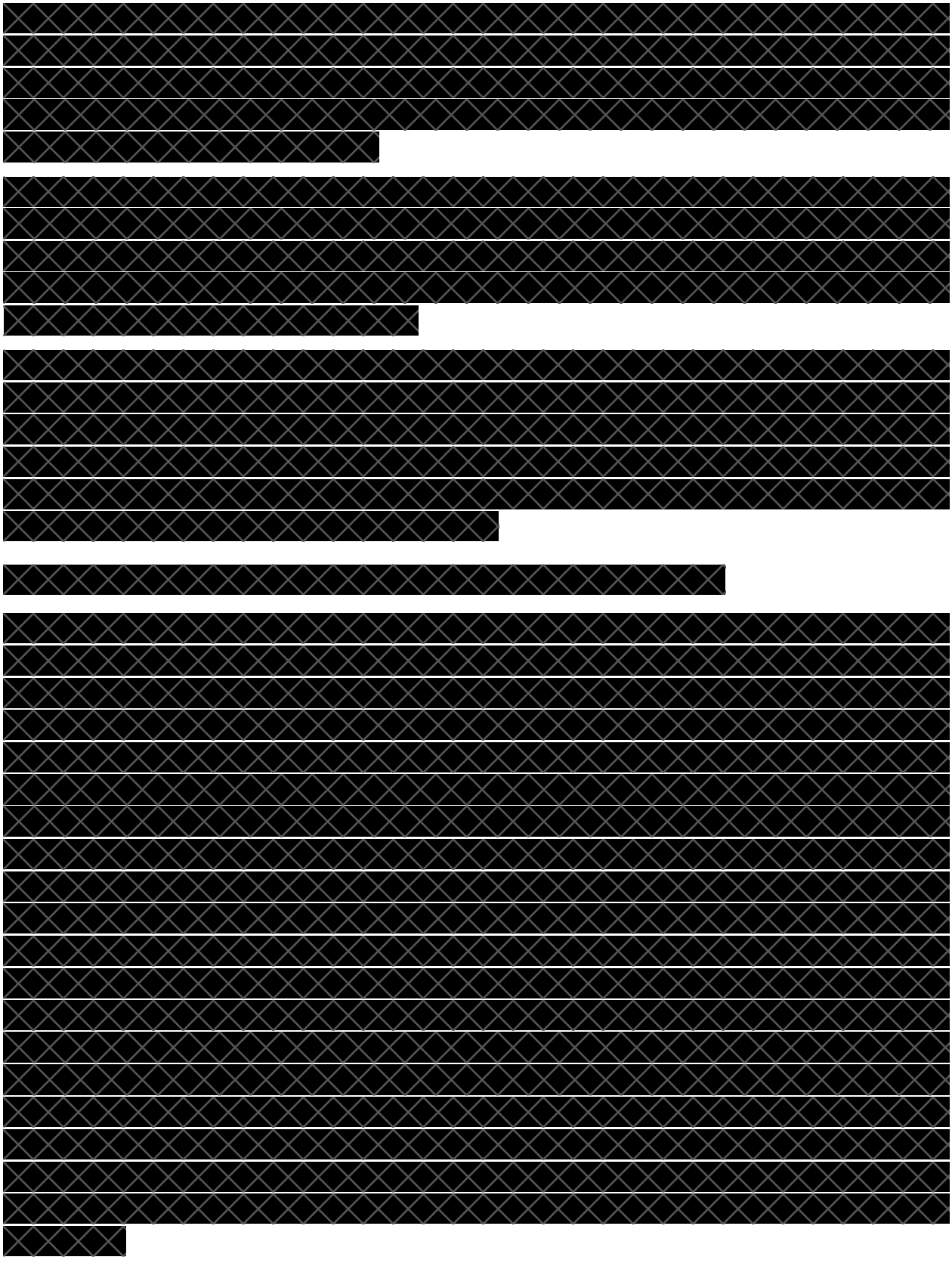






4. STUDY OBJECTIVES

4.1 PRIMARY OBJECTIVES

The primary objectives of this study are:

- To determine the objective response rate (ORR) per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the safety and tolerability of the combination of AB-16B5 and docetaxel

4.2 SECONDARY OBJECTIVES

The secondary objectives of this study are:

- To determine the clinical benefit rate (complete response (CR), partial response (PR) and stable disease (SD)) per RECIST 1.1 and the duration of clinical benefit in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the duration of response (CR and PR) per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the duration of stable disease per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the progression free survival (PFS) per RECIST 1.1 in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the overall survival (OS) in subjects receiving the combination of AB-16B5 and docetaxel
- To determine the pharmacokinetics of AB-16B5 in this subject population

[redacted]

5. STUDY DESIGN

This is an open-label, single-arm, multi-center Phase II trial of AB-16B5 in combination with docetaxel in previously treated subjects with metastatic non-small cell lung cancer who have experienced disease progression following treatment with a platinum-containing doublet treatment and an anti-PD1 or PD-L1 immune checkpoint antibody, administered simultaneously or

sequentially. Approximately 40 subjects will be enrolled in this trial and receive AB-16B5 at a dose of 12 mg/kg once weekly on Days 1, 8 and 15 combined with docetaxel at a dose of 75 mg/m^2 once every 3 weeks on Day 1. One cycle of treatment will consist of 21 days (3 weeks). The safety profile of the AB-16B5 and docetaxel combination will be examined during a safety lead-in period with the first 8 subjects completing one cycle of treatment or experiencing a DLT during Cycle 1 and being part of the DLT Evaluable population (as defined in Section 12.4.4).

Radiographic imaging will be performed every 6 weeks until disease progression to assess response to treatment using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria for determination of the objective response rate (ORR) and progression free survival (PFS). A futility analysis will be conducted to minimize subject exposure to an ineffective treatment. Paired tumor biopsies (pre-treatment and on-treatment) will be collected in all subjects. Adverse events will be monitored throughout the study and graded for severity according to the NCI Common Terminology Criteria for Adverse Events (CTCAE). Study treatment will continue until there is evidence of disease progression (defined according to RECIST 1.1), treatment-related adverse events of unacceptable severity, subject request for discontinuation or Investigator determination that further treatment is not in the subject's best interest. Treatment beyond progression will be allowed if the Investigator considers the subject to be clinically stable (see Section 7.2 for definition of clinically stable).

Subjects who must discontinue AB-16B5 or docetaxel due to toxicity or any reasons other than progressive disease will continue on the other treatment (AB-16B5 or docetaxel). Subjects who must discontinue both AB-16B5 and docetaxel for reasons other than progressive disease will remain in the study to obtain tumor imaging until disease progression.

5.1 SAFETY LEAD-IN PERIOD

The safety profile of AB-16B5 at a dose of 12 mg/kg administered once weekly on Days 1, 8 and 15 combined with docetaxel at a dose of 75 mg/m^2 once every 3 weeks on Day 1 will be examined during a safety lead-in period with the first 8 subjects completing one cycle of treatment or experiencing a DLT during Cycle 1 and being part of the DLT Evaluable population. No dose escalation will be performed but a decision to de-escalate the dose of AB-16B5 could be made using the modified toxicity probability interval method (mTPI)[2].

The study treatment will be considered acceptable if no more than 3 subjects experienced a DLT during the first cycle in the first 8 subjects treated.

For these purposes, a DLT will be defined as a Grade ≥ 3 non-hematologic toxicity occurring during Cycle 1 of therapy. In addition, the following hematologic toxicities will be considered as a DLT:

- Grade ≥ 4 neutropenia or thrombocytopenia > 7 days
- Grade ≥ 3 thrombocytopenia with bleeding

- Grade ≥ 3 febrile neutropenia

Toxicities that are clearly and incontrovertibly due to disease progression or to extraneous causes will not be considered DLTs. In addition, the following non-hematologic toxicities will not be considered DLTs:

- Grade 3 arthralgia or myalgia which returns to Grade ≤ 1 within < 7 days with appropriate supportive care
- Grade 3 nausea, vomiting or diarrhea which returns to Grade ≤ 1 within < 72 hours with appropriate supportive care
- Grade 3 fatigue lasting < 7 days
- Grade 3 electrolyte abnormalities that last less than 72 hours and are not associated with clinical symptoms
- Grade 3 amylase or lipase elevation which is not associated with symptoms or clinical manifestations of pancreatitis

De-escalation of AB-16B5 will be performed if more than 3 subjects experienced a DLT in the first 8 subjects treated.

The next three subjects will then be treated with AB-16B5 at 9 mg/kg AB-16B5 administered once weekly on Days 1, 8 and 15 combined with docetaxel at a dose of 75 mg/m^2 once every 3 weeks on Day 1. If 0 or 1 subject experienced a DLT during the first cycle in these 3 subjects, AB-16B5 at the 9 mg/kg dose will be considered acceptable.

If more than 1 subject experienced a DLT, a final de-escalation of AB-16B5 to 6 mg/kg will be performed and the safety profile will be evaluated using the same process as described above.

5.2 FUTILITY ANALYSIS

A futility analysis will also be conducted with a minimum of 10 evaluable subjects (i.e., subjects who are part of the Clinical Activity Evaluable Population as defined in Section 12.4.1). Monitoring of responses will be done every 8 subjects thereafter until up to 34 evaluable subjects are obtained or the trial is stopped for futility. The trial will be stopped for futility if either 0 confirmed response out of 10 subjects, 1 confirmed response out of 18, 2 confirmed responses out of 26 or 6 confirmed responses out of 34 are obtained. If more than 6 confirmed responses are obtained out of 34 evaluable subjects, AB-16B5 in combination with docetaxel will be considered promising.

Futility will be assessed once the number of evaluable patients is obtained at each review of the data. If the confirmation of a response is crucial for the decision making (e.g., if there is only one unconfirmed response out of the 10 first evaluable patients), the decision to stop for futility will be postponed until there is a second scan for confirmation. A detailed set of rules and review

timelines will be presented in a futility assessment charter which will be completed prior to the enrollment of the tenth patient in the study.

5.3 DATA SAFETY MONITORING BOARD

A Data Safety Monitoring Board (DSMB) composed of an independent oncologist, the Principal Investigator, the medical monitor, the biostatistician and a sponsor representative will meet to review the safety lead-in data and to determine the safe dose to continue the study enrollment.

6. INCLUSION AND EXCLUSION CRITERIA

6.1 INCLUSION CRITERIA

Subjects enrolled in the study must meet the following inclusion criteria:

1) Subjects (male or non-pregnant female) must be ≥ 18 years of age on the day of signing the informed consent.
2) Subjects with a histologically or cytologically confirmed diagnosis of (Stage III-IV) non-small cell lung cancer (NSCLC) and with at least one measurable lesion defined by RECIST 1.1.
3) Subjects must have experienced a disease progression following treatment with an anti-PD1 or PD-L1 immune checkpoint antibody and a platinum-containing doublet treatment, administered simultaneously or sequentially.
4) Subjects with a targetable driver mutation in EGFR or ALK gene will be allowed on trial after failing all available targeted therapies and having experienced a disease progression following treatment with an anti-PD1 or PD-L1 immune checkpoint antibody and a platinum-containing doublet treatment, administered simultaneously or sequentially.
5) Subjects must have adequate organ and immune function as indicated in the table below:

System	Laboratory Value
Hematological	
Absolute neutrophil count (ANC)	≥ 1.5 X 10^9/L (1,500 cells/mm^3)
Platelets	≥ 100 X 10^9/L (100,000 cells/mm^3)
Hemoglobin	≥ 90 g/L
Hepatic	
Total bilirubin	≤ ULN
AST (SGOT) and ALT (SGPT)	≤ 1.5 X ULN, unless secondary to liver metastases
Alkaline phosphatase	≤ 2.5 X ULN
Renal	

Creatinine clearance[a]	≥ 50 mL/min
Coagulation	
International Normalized Ratio (INR)	≤ 1.5 X ULN[b]
[a]Creatinine clearance should be calculated using the Cockcroft-Gault Method: Formula to use when serum creatinine is expressed in mg/dL: CrCl = [(140-age) X weight (kg) X (0.85 for females only)] / (72 X serum creatinine (mg/dL)) Formula to use when serum creatinine is expressed in μmol/L: CrCl = 1.23 X [(140-age) X weight (kg) X (0.85 for females only)] / (serum creatinine (μmol/L)) [b]if subject is receiving anticoagulant therapy, then INR must be within therapeutic range.	

6) Subjects must have a tumor lesion amenable for biopsies with no contraindication for biopsy.
7) Subjects must have an Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2.
8) Subjects must have a life expectancy of at least 3 months.
9) Subjects must have recovered from the toxic effects resulting from the most recent cancer treatment to Grade 1 or less. If the subjects underwent major surgery or received radiation therapy, they must have recovered from the complications and/or toxicity.
10) Female subjects of childbearing potential must have a negative serum pregnancy test within 72 hours prior to the first dose of study treatment.
11) Subjects (both male and female) of reproductive potential must be willing to practice highly effective methods of contraception throughout the study and for up to 90 days after the last dose of study medication. Abstinence is acceptable if this is the subject's usual lifestyle.
12) Female subjects are not considered of childbearing potential if they have a history of surgical sterility or evidence of post-menopausal status defined as any of the following:
    - ≥ 45 years of age and has not had menses for more than 2 years.
    - Amenorrhoeic for < 2 years without hysterectomy and oophorectomy and a follicle stimulating hormone (FSH) value in the postmenopausal range at screening.
    - Post hysterectomy, oophorectomy or tubal ligation. Documented hysterectomy or oophorectomy must be confirmed with medical records of the actual procedure or by ultrasound. Tubal ligation must be confirmed with medical records of the actual procedure.
13) Subjects must understand and be able and willing and likely to fully comply with the study procedures, including scheduled follow-up, and restrictions.
14) Subjects must have given written personally signed and dated informed consent to participate in the study in accordance with the International Conference on Harmonization

(ICH) Good Clinical Practice (GCP) Guidelines, before completing any study related procedures.

6.2 EXCLUSION CRITERIA

Subjects enrolled in the study must not meet the following exclusion criteria:

1) Subjects who have received prior therapy with AB-16B5.
2) Subjects who have received prior therapy with docetaxel for the treatment of NSCLC.
3) Subjects who are currently participating or has participated in a study of an investigational agent or using an investigational device within 21 days prior to the first dose of study treatment. The 21-day window should be calculated using the last dose of an antineoplastic investigational agent or last use of an investigational device with antineoplastic intent.
4) Subjects who have received any anti-cancer treatment within 3 weeks or radiation therapy within 2 weeks prior to receiving the first dose of study treatment or who have not recovered from adverse events to Grade 1 or less. Subjects with alopecia are eligible to participate.
5) Subjects who are expected to require any other form of systemic or localized antineoplastic therapy while on the trial. This includes maintenance therapy with another agent or radiation therapy.
6) Subjects who are receiving a dose > 10 mg/day of prednisone (or equivalent) within 7 days prior to the first dose of study treatment or any other form of immunosuppressive medication (corticosteroid pre-treatment and/or post-treatment of docetaxel is allowed).
7) Subjects who require treatment with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole). Subjects may be included if there is an alternate treatment with a weak CYP3A4 inhibitor and they are willing to change at least 7 days prior to the first dose of study treatment.
8) Subjects who have another malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin or in situ cervical cancer.
9) Subjects who have known active central nervous system metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate if they have been clinically stable for at least 2 weeks prior to the first dose of study treatment, if they have no evidence of new or enlarging brain metastases and if they are not receiving a dose > 10 mg/day of prednisone (or equivalent) within 7 days prior to the first dose of study treatment.
10) Subjects with clinically significant ECG abnormalities.

11) Subjects who have received or will receive a live vaccine within 30 days prior to the first dose of study treatment.

12) Subjects with a known history of human immunodeficiency (HIV).

13) Subjects with an active Hepatitis B or C infection.

14) Subjects with an active infection requiring antibiotic therapy.

15) Subjects with a known history of alcohol or other substance abuse within the last year.

16) Subjects with known hypersensitivity to docetaxel or drugs formulated with polysorbate 80.

17) Subjects who have a history or current evidence of any condition, therapy or laboratory abnormalities that may confound the results of the trial, interfere with the subject's participation for the full duration of the trial or if it is not in the best interest of the subject to participate in the trial.

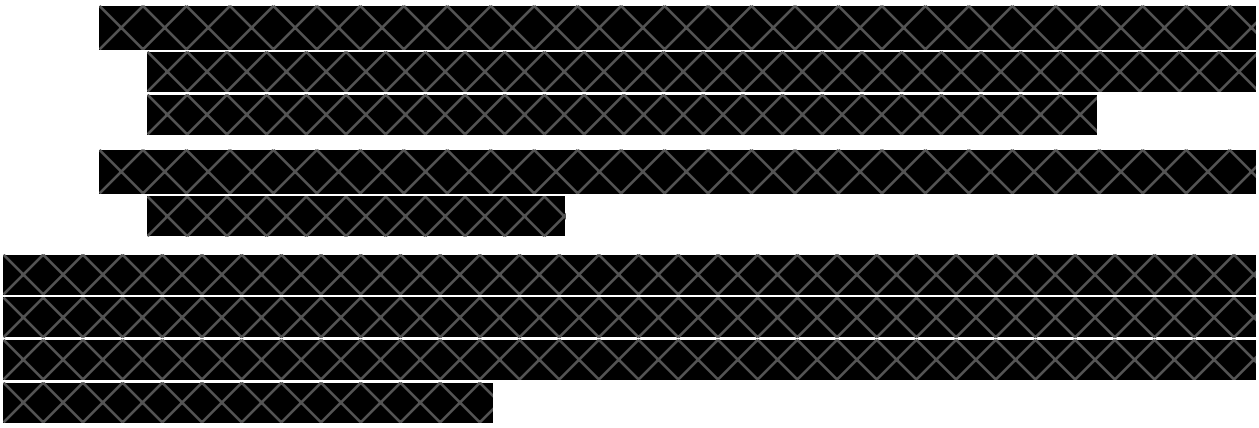
18) Subjects with medical, social or psychosocial factors that, in the opinion of the treating Investigator, could impact the safety or compliance with study procedures.

19) Subjects who are pregnant or lactating or who are expecting to conceive or father children within the projected duration of the trial through 90 days after the last dose of AB-16B5 or the last dose of docetaxel.

7. STUDY TREATMENT

7.1 [redacted]

[redacted]



7.1.2 Docetaxel

Docetaxel will be administered at the dosage of 75 mg/m^2 by a 60-minute IV infusion once every 3 weeks on Day 1. Docetaxel will be prepared and administered as per approved product label/monograph and hospital standard practices.

All subjects should be premedicated with corticosteroids as per hospital standard practices. Vein extravasation and accidental spillages should be dealt with according to the hospital standard practices.

7.2 TREATMENT DURATION

One cycle of treatment will consist of 21 days (3 weeks).

Study treatment will continue until there is evidence of disease progression, unacceptable toxicity, subject requests discontinuation of study treatment, or the Investigator feels that further treatment is not in the subject's best interest. Subjects who must discontinue AB-16B5 or docetaxel due to toxicity or any reasons other than progressive disease may continue on the other treatment (AB-16B5 or docetaxel).

Treatment beyond progression will be allowed if the Investigator considers the subject to be clinically stable. The clinical judgment decision by the site should be based on the clinical stability of the subjects as defined below:

Clinical stability is defined as the following:

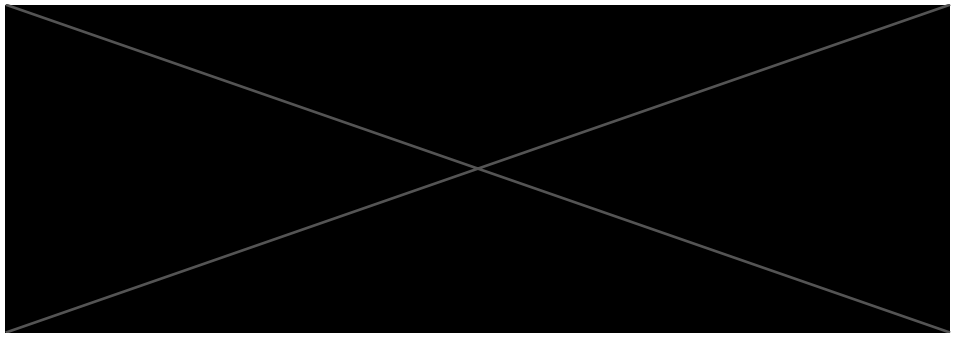
- Absence of symptoms and signs indicating clinically significant progression of disease, including worsening of laboratory values
- No decline in ECOG performance status
- Absence of rapid progression of disease
- Absence of progressive tumor at critical anatomical sites (e.g., cord compression) requiring urgent alternative medical intervention

Any subject deemed clinically unstable should be discontinued from trial treatment at first radiologic evidence of PD.

Subjects who must discontinue both AB-16B5 and docetaxel for reasons other than progressive disease will remain in the study to obtain tumor imaging until disease progression.

7.3 STUDY TREATMENT DOSE REDUCTION

[redacted]



[redacted]

7.3.2 Docetaxel Dose Reduction

Subjects who experience either febrile neutropenia, neutrophils < 500 cells/mm^3 for more than one week, severe or cumulative cutaneous reactions, or other Grade ≥ 3 non-hematological toxicities that is judged to be related to docetaxel should have treatment withheld until resolution of the toxicity and then resumed at 60 mg/m^2. Based upon subject's condition, treatment with AB-16B5 may continue during this cycle and the start of a new cycle could be delayed by one week. In this case, a fourth dose of AB-16B5 would be administered in the cycle.

Subjects who develop Grade ≥ 3 peripheral neuropathy should have docetaxel discontinued.

7.4 AB-16B5 AND DOCETAXEL DRUG ACCOUNTABILITY

Accurate records of all drug shipments reconstituted and dispensed AB-16B5, and record of all drug that is returned must be accounted for on an AB-16B5 Study Drug Accountability Form provided to the Investigator by the Sponsor. This inventory record must be available for inspection

by the Study Monitor during regular monitoring visits. AB-16B5 Drug supplies are to be used only in accordance with this protocol and under the supervision of the Investigator.

Any study drug requiring destruction must be destroyed according to the hospital standard practices. At the end of the study, the final drug accountability reconciliation will take place. The overall number of vials shipped to the center, and the number of vials destroyed or returned will be provided by the pharmacy, and an account given of any discrepancy.

Docetaxel accountability should also be maintained as per the hospital standard practice.

8. STUDY FLOW CHART

The Study Flow Chart (Table 5) summarizes the trial procedures to be performed at each visit. Individual trial procedures are described in detail below. It may be necessary to perform these procedures at unscheduled time points if deemed clinically necessary by the Investigator.

Furthermore, additional evaluations/testing may be deemed necessary by the Investigator and or the Sponsor for reasons related to subject safety. In these cases, such evaluations/testing will be performed as per standard clinical practices.

Table 5: Schedule of Study Procedures/Assessments

	Screening Phase	Treatment Cycles (21-Day Cycles)[1]								End of Treatment	Post-Treatment[3]	
Treatment Cycle	**Screening**	**1[2]**	**2[2]**	**3[2]**	**4[2]**	**5[2]**	**6[2]**	**7[2]**	**8 and beyond[2]**	**Discontinuation (DC)**	**Safety Follow-Up**	**Survival Follow-Up**
Scheduling Window (Days)	**-28 to -1**									**At time of DC**	**30 Days Post Last Treatment**	**Every 12 Weeks**
Informed Consent	x											
Inclusion/Exclusion Criteria	x											
Demographics and Medical History	x											
Prior and Concomitant Medications	x	x	x	x	x	x	x	x	x	x	x	x
NSCLC Disease and Prior Treatment	x											
Subsequent Anti-Cancer Treatment											x	x
Survival Status												x
Clinical Procedures/Assessments												
Review of Adverse Events		x	x	x	x	x	x	x	x	x	x	x
Complete Physical Examination	x									x		
Directed Physical Examination		x	x	x	x	x	x	x	x			
Vitals Signs[4]	x	x	x	x	x	x	x	x	x	x		
Body Weight	x	x	x	x	x	x	x	x	x	x		
Height	x											
12-Lead ECG[5]	x											
ECOG	x	x	x	x	x	x	x	x	x	x	x	
Efficacy Measurement												
Tumor Imaging[6]	x		x		x		x		x	x		
[redacted]												
Laboratory Procedures/Assessments (Local Laboratory)												
Pregnancy Test[8]	x									x		
Coagulation Test	x											
Hematology	x	x[9]	x	x	x	x	x	x	x	x		
Clinical Biochemistry	x	x[9]	x	x	x	x	x	x	x	x		
Urinalysis	x		x		x		x		x[10]			
Laboratory Procedures/Assessments (Central Laboratory)												
AB-16B5 Pharmacokinetics[11]		x	x		x				x[11]			
Anti-AB-16B5 Antibodies[12]		x	x		x				x[12]	x		

Study Treatment Administration												
AB-16B5[13]		x	x	x	x	x	x	x	x			
Docetaxel[14]		x	x	x	x	x	x	x	x			

9. STUDY PROCEDURES

9.1 SUBJECT INFORMED CONSENT

The Investigator must obtain documented consent from each potential subject or each subject's legally acceptable representative prior to participating in a clinical study.

Informed consent form must be documented by the subject's dated signature or by the subject's legally acceptable representative's dated signature on a consent form along with the dated signature of the person conducting the consent discussion. A copy of the signed and dated informed consent form should be given to the subject before participation in the study.

The initial informed consent form, any subsequent revised written informed consent form and any written information provided to the subject must receive the IRB/EC's approval/favorable opinion in advance of use. The subject or his/her legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the study. The communication of this information will be provided and documented via a revised consent form or addendum to the original consent form that captures the subject's dated signature or by the subject's legally acceptable representative's dated signature.

The informed consent will adhere to IRB/EC requirements, applicable laws and regulations and Sponsor requirements.

9.2 INCLUSION/EXCLUSION CRITERIA

All inclusion and exclusion criteria will be reviewed by the Investigator to ensure that the subject qualifies for the study.

9.3 MEDICAL HISTORY

A medical history will be obtained by the Investigator. Medical history will include all active conditions and any condition diagnosed within the prior 10 years that are considered to be clinically significant by the Investigator.

The Investigator will obtain prior and current details regarding the subject's lung cancer. These details will be recorded separately and not listed as medical history.

9.4 PRIOR AND CONCOMITANT MEDICATIONS

9.4.1 Prior Medications

The Investigator will review and record prior medication taken by the subject within 1 month prior to study treatment start.

The Investigator will review and record all prior anti-cancer treatments including systemic treatments, radiation, and surgeries, regardless of the time prior to first dose of trial treatment.

Prior anti-cancer treatment for NSCLC will be recorded separately and not listed as a prior medication.

9.4.2 Concomitant Medications

The Investigator will record all concomitant medications taken by the subjects during the study.

The subject must not receive other anti-cancer therapy or investigational drugs while on study. Palliative radiotherapy may be given; however, the irradiated lesions will not be evaluated for response. Supportive treatments will be given according to label instructions as medically indicated for subjects.

During the post-treatment period, only concomitant medications related to adverse events requiring a follow-up will be recorded.

9.4.3 Subsequent Anti-Cancer Treatment

The Investigator will review all new anti-cancer therapy initiated after the last dose of study treatment. If a subject initiates a new anti-cancer therapy within 30 days after the end of treatment, the 30-day Safety Follow-Up visit must occur before the first new dose of the new therapy. Once new anti-cancer therapy has been initiated, the subject will move into Survival Follow-Up.

9.5 ADVERSE EVENT MONITORING

Safety will be assessed by physical examination, measurement of vital signs, clinical laboratory evaluations and electrocardiogram. Clinically significant changes in these parameters will be captured as adverse events (AEs).

The Investigator is responsible for the appropriate medical care and the safety of subjects who have entered this study. The Investigator must document all AEs and notify the Sponsor of any serious adverse event (SAE) experienced by subjects who have entered this study.

Refer to Section 11 for detailed information regarding the assessment and recording of AEs.

9.6 PHYSICAL EXAMINATION

9.6.1 Complete Physical Examination

The Investigator will perform a complete physical exam during the screening period. Clinically significant abnormal findings should be recorded as medical history. After the first dose of trial treatment, new clinically significant abnormal findings should be recorded as AEs. A complete physical exam will also be performed at the end of treatment.

9.6.2 Directed Physical Examination

For treatment cycles, the Investigator will perform a directed physical exam as clinically indicated prior to trial treatment administration. New clinically significant abnormal findings should be recorded as AEs.

9.7 VITAL SIGNS, BODY WEIGHT AND HEIGHT

Vitals signs will be measured at screening, within 48 hours prior to each study treatment administration (i.e., Day 1, Day 8 and Day 15 of each cycle) and at the end of treatment. Vital signs will include temperature, pulse, respiratory rate and blood pressure. Body weight will be measured at screening, within 48 hours prior to Day 1 of each cycle and at the end of treatment. Height will be measured at screening only.

9.8 ELECTROCARDIOGRAM (ECG)

12-lead ECG assessments will be performed after resting for 5 minutes and will include heart rate, PR, QRS, RR, QT, QTc. This test will be performed at screening only. Additional 12-lead ECG assessments may be performed as clinically indicated.

9.9 EASTERN COOPERATIVE ONCOLOGY GROUP (ECOG) PERFORMANCE SCALE

The Investigator will assess ECOG status at screening, within 48 hours prior to the study treatment administration on Day 1 of each cycle, at the end of treatment and during the Safety Follow-Up.

9.10 TUMOR IMAGING AND ASSESSMENT OF DISEASE

Tumor imaging should be acquired by computed tomography (CT, strongly preferred). Magnetic resonance imaging (MRI) should be used when CT is contraindicated or for imaging in the brain. The same imaging technique regarding modality and use of contrast should be used in a subject throughout the trial to optimize the visualization of existing and new tumor burden.

Local site Investigator/radiology assessment based on RECIST 1.1 will be used to determine subject eligibility.

9.10.1 Initial Tumor Imaging

Initial tumor imaging at screening must be performed within 28 days prior to the study treatment start. The site study team must review screening images to confirm the subject has measurable disease per RECIST 1.1.

Scans performed as part of routine clinical management are acceptable for use as screening tumor imaging if they are of diagnostic quality and performed within 28 days prior to the date of study treatment start.

9.10.2 Tumor Imaging During the Trial

Tumor assessments during study treatment will be performed every 6 weeks at the end (between Day 16 and Day 21) of every even numbered cycle of treatment (i.e., Cycles 2, 4, 6, etc.) or more frequently if clinically indicated.

In subjects who discontinue the study treatment due to documented disease progression, no additional tumor imaging is required.

Subjects who discontinue both AB-16B5 and docetaxel for reasons other than progressive disease will be re-evaluated at the time of treatment discontinuation unless a tumor assessment was performed within the previous four weeks. Additional tumor imaging will then be performed approximately every 6 weeks after the last tumor imaging until disease progression (unless the Investigator elects to continue treatment beyond progression), the start of new anti-cancer treatment or withdrawal of consent, whichever occurs first.

Partial and complete response should be confirmed by a repeat tumor imaging assessment. The tumor imaging for confirmation of response will be performed at the earliest 4 weeks after the first indication or at the next scheduled scan, whichever is clinically indicated.

9.10.3 Assessment of Disease by RECIST 1.1

RECIST 1.1 will be used as the primary measure for assessment of the objective response rate (ORR), clinical benefit rate, duration of response, duration of stable disease and progression free survival (PFS).

9.12 SAFETY LABORATORY EVALUATIONS

Clinical laboratory tests will be performed locally at the clinical center. Laboratory tests for screening must be performed within 28 days prior to the first dose of study treatment. A serum pregnancy test will be done within 72 hours prior to the first cycle of treatment (Cycle 1) and at the end of treatment for all females with an intact uterus, regardless of age, unless amenorrhoeic for the previous 12 months. A coagulation test will be performed at screening only. However, subjects receiving anticoagulant therapy must be monitored closely during the study.

During Cycle 1, hematology and clinical biochemistry will be performed within 48 hours prior to each study treatment administration (i.e., Day 1, Day 8 and Day 15). From Cycle 2 and onward, hematology and clinical biochemistry will be performed within 48 hours prior to the study treatment administration on Day 1 only. Urinalysis will be performed at every 2 cycles.

Laboratory results must be known and acceptable prior to dosing on Day 1 of each cycle.

The following laboratory parameters will be evaluated:

Hematology	Clinical Biochemistry	Urinalysis	Other
Absolute neutrophil count	Albumin	Blood	INR
Hemoglobin	Alkaline phosphatase	Glucose	aPTT/PTT
Hematocrit	ALT	Microscopic exam (if abnormal results are noted)	
Platelet count	Amylase		
Red blood cell count	AST	Protein	
White blood cell count (total and differential)	Bicarbonate	Specific gravity	
	Calcium		
	Chloride		
	Creatinine		
	Creatinine clearance		
	Glucose		
	Lipase		
	Magnesium		
	Phosphate		
	Potassium		
	Sodium		
	Total Bilirubin		
	Total Protein		
	Urea		
	Uric acid		

9.13 PHARMACOKINETIC/PHARMACODYNAMIC EVALUATIONS

9.13.1 Blood Collection for Plasma AB-16B5

Blood samples (approximately 10 mL per sample) for the assay of AB-16B5 will be collected from all subjects to define the pharmacokinetic properties of AB-16B5 when administered intravenously once weekly. Blood samples will be collected throughout the study at the following time-points:

Cycle	Day	Time-point
1	1	Prior to starting AB-16B5 infusion
		0.5 hour after starting AB-16B5 infusion
		1 hour (immediately prior to the end of AB-16B5 infusion)
		2 hours after starting AB-16B5 infusion
	3	48 hours after starting AB-16B5 infusion
	8	Prior to starting AB-16B5 infusion
		0.5 hour after starting AB-16B5 infusion
		1 hour (immediately prior to the end of AB-16B5 infusion)
	15	Prior to starting AB-16B5 infusion
		0.5 hour after starting AB-16B5 infusion
		1 hour (immediately prior to the end of AB-16B5 infusion)
2	1	Prior to starting AB-16B5 infusion
		0.5 hour after starting AB-16B5 infusion
		1 hour (immediately prior to the end of AB-16B5 infusion)
		2 hours after starting AB-16B5 infusion
	8	Prior to starting AB-16B5 infusion
		0.5 hour after starting AB-16B5 infusion
		1 hour (immediately prior to the end of AB-16B5 infusion)
	15	Prior to starting AB-16B5 infusion
		0.5 hour after starting AB-16B5 infusion
		1 hour (immediately prior to the end of AB-16B5 infusion)
	16-21	On the day of the scan or the biopsy
4	1	Prior to starting AB-16B5 infusion
8	1	Prior to starting AB-16B5 infusion
Every 4 cycles thereafter	1	Prior to starting AB-16B5 infusion

There will be no pharmacokinetic blood samples collected beyond Cycle 36. Clinical staff is encouraged to take the blood samples at the scheduled time-point; however, deviations from the scheduled sample times are not considered protocol deviations. Blood should not be collected from

the same vein used to administer AB-16B5. Samples should be stored at the clinical site at -70°C until shipment to the assigned bioanalytical laboratory for analysis.

9.13.2 Blood Collection for Anti-AB-16B5 Antibodies

Blood samples (approximately 5 mL per sample) will be collected from all subjects to determine the presence of anti-AB-16B5 antibodies (ADA).

Anti-AB-16B5 antibody (ADA) samples will be collected prior to the infusion of AB-16B5 on Day 1, Day 8 and Day 15 of Cycle 1, on Day 1 of Cycles 2 and 4 and on Day 1 of every 4 cycles thereafter. An ADA sample will also be collected at the End of Treatment visit.

Cycle	Day	Time-point
1	1	Prior to starting AB-16B5 infusion
	8	Prior to starting AB-16B5 infusion
	15	Prior to starting AB-16B5 infusion
2	1	Prior to starting AB-16B5 infusion
4	1	Prior to starting AB-16B5 infusion
Every 4 cycles thereafter	1	Prior to starting AB-16B5 infusion

There will be no ADA blood samples collected beyond Cycle 36. Similarly, no ADA blood samples will be collected at End of Treatment visit for subjects continuing treatment beyond Cycle 36. Samples should be stored at the clinical site at -70°C until shipment to the assigned bioanalytical laboratory for analysis.

[redacted]

10. VISIT REQUIREMENTS

10.1 SCREENING

Visit requirements are outlined in Section 8 - Study Flow Chart. Specific procedure-related details are provided above in Section 9 - Study Procedures.

Approximately 28 days prior to randomization, potential subjects will be evaluated to determine that they fulfill the entry requirements as set forth in Section 6. Screening procedures may be repeated after consultation with the Sponsor.

Written consent must be obtained prior to performing any protocol specific procedure. Results of a test performed prior to the subject signing consent as part of routine clinical management are acceptable in lieu of a screening test if performed within the specified time frame. Screening

procedures are to be completed within 28 days prior to the first dose of study treatment except for the following:

- For women of reproductive potential, a pregnancy test will be performed within 72 hours prior to first dose of study treatment.

10.2 TREATMENT CYCLES

Visit requirements are outlined in Section 8 - Study Flow Chart. Specific procedure-related details are provided above in Section 9 - Study Procedures.

10.3 END OF TREATMENT

The End of Treatment visit should be conducted when both AB-16B5 and docetaxel are discontinued. Visit requirements are outlined in Section 8 - Study Flow Chart. Specific procedure-related details are provided above in Section 9 - Study Procedures.

10.4 POST-TREATMENT

10.4.1 Safety Follow-Up

The mandatory Safety Follow-Up Visit should be conducted approximately 30 days (± 7 days) after the last dose of study treatment or before the initiation of a new anti-cancer treatment, whichever comes first.

10.4.2 Survival Follow-Up

Survival Follow-Up contacts by telephone will be made every 12 weeks (± 2 weeks) after the Safety Follow-Up Visit to assess survival for survival status. Subjects with a related AE of Grade ≥ 2 will be further followed until the resolution of the AE to Grade ≤ 1 or until beginning of a new anti-cancer treatment, whichever occurs first. Survival Follow-Up contacts will continue until either death, withdrawal of consent, or the end of the study, whichever occurs first.

11. ADVERSE EVENT REPORTING

11.1 DEFINITIONS

Adverse Event (AE): Any unfavorable or unintended sign, symptom, or disease that is temporally associated with the use of a study treatment but is not necessarily caused by the study treatment. This includes worsening (e.g., increase in frequency or severity) of pre-existing conditions.

Serious Adverse Event (SAE): An adverse event resulting in any of the following outcomes:

- death
- is life-threatening (i.e. an immediate threat to life)
- insubject hospitalization*
- prolongation of an existing hospitalization

- persistent or significant disability/incapacity
- congenital anomaly/birth defect
- is medically important[+]

*An insubject hospitalization is defined as an admission for any length of time. A hospitalization for the administration of study treatment, for routine or planned clinical procedures, or for "social" reasons (not the result of any adverse change in the subject's condition) should not be considered an adverse event and should not be reported as a serious adverse event. If the subject experiences any adverse change in condition during hospitalization, the condition must be reported as an adverse event or serious adverse event according to the above definitions.

[+]Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or result in hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed above.

Unexpected Adverse Event: An adverse event, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator's Brochure for an unapproved study agent or package insert/summary of product characteristics for an approved product). Expected means that the event has previously been observed with the study treatment and is identified and/or described in the applicable product information. It does not mean that the event is expected with the underlying disease(s) or concomitant medications.

11.2 REPORTING ADVERSE EVENTS TO THE SPONSOR

All adverse events that are identified from the start of study treatment administration (Day 1) through 30 days following administration of the last dose of study treatment will be recorded on the Adverse Event Electronic Case Report Form (AE eCRF). All data fields on the AE eCRF must be completed.

Serious Adverse Events must also be recorded on the SAE Worksheet and sent to the Drug Safety designee within 24 hours of site personnel becoming aware of the SAE. The SAE Worksheet should be completed as much as possible but should not be held until all information is available. Additional information, follow-up information, and corrections should be provided on subsequent updates of the SAE Worksheet that are clearly identified as follow-up (#1, #2, etc.) reports. The SAE Worksheets should be sent to the Sponsor using the Drug Safety contact information and process as provided on the SAE Worksheet.

Drug Safety personnel will be available to answer questions and assist site personnel in documenting SAEs and completing the SAE worksheet.

11.3 LABORATORY ABNORMALITIES AS ADVERSE EVENTS

A laboratory abnormality should be reported as an adverse event if it is associated with an intervention. Intervention includes, but is not limited to, discontinuation of treatment, dose

reduction/delay, or concomitant therapy. In addition, any medically important laboratory abnormality may be reported as an adverse event at the discretion of the Investigator. This includes laboratory abnormalities for which there is no intervention, but the abnormal value(s) suggests a disease or organ toxicity. If clinical sequelae are associated with a laboratory abnormality, the diagnosis or medical condition should be reported (e.g., renal failure, hematuria) not the laboratory abnormality (e.g., elevated creatinine, urine RBC increased).

11.4 REPORTING A PREGNANCY

All pregnancies are reported up to 30 days following the last dose of study treatment. A pregnancy must be reported to the Drug Safety designee as soon as the site becomes aware of the pregnancy. The Drug Safety designee will send an acknowledgement memorandum to the Investigator along with a Pregnancy Assessment Form. A follow-up Pregnancy Assessment Form will be sent to the site every 3 months. Pregnancy Assessment Forms must be completed by the Investigator until delivery, elective termination of the pregnancy, or miscarriage. The Investigator is responsible for following the subject's pregnancy to final outcome.

Pregnancies are not considered adverse events. Complications or medical problems associated with a pregnancy are considered AEs and may be SAEs. Complications or medical problems are reported as AEs/SAEs if they occur during the study follow-up period (30 days after the last dose of study treatment) according to the procedure described in Section 11.2.

11.5 INVESTIGATOR EVALUATION OF ADVERSE EVENTS

Severity will be graded using the NCI CTCAE Version 5.0. The CTCAE Version 5.0 may be downloaded from the Cancer Treatment Evaluation Program (CTEP) website (https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf). In the event that an AE does not have a CTCAE code, the following severity classifications will be used:

Severity:

Grade	Severity	Description
1	Mild	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
2	Moderate	Minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL). Instrumental ADL refer to preparing meals, shopping for groceries and clothes, using the telephone, managing money, etc.
3	Severe	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL. Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.
4	Life-threatening*	Life-threatening consequences; urgent intervention indicated.

Grade	Severity	Description
5	Death	Death related to AE.

*Note – a severity assessment of life-threatening is not necessarily the same as the seriousness criterion of life-threatening. The former means that the event is a potential threat to life. The latter means that the event is an immediate threat to life.

Causality:

For each AE, the Investigator should determine and document whether there exists a reasonable possibility that any component of the study treatment caused or contributed to the AE. The Investigator's assessment should be recorded in the source document. If the Investigator does not know whether or not the study treatment is causally related to the event, reporting for study purposes will be as at least "possibly related" to study treatment. The initial causality assessment may be revised as new information becomes available (see table below).

Relationship to Drug	Description
Definitely Related	Exhibits previously known toxicity of agent; or Follows a reasonable temporal sequence from administration of the drug; Follows a known or expected response pattern to the suspected drug; Is confirmed by stopping or reducing the dosage of the drug; and Is not explained by any other reasonable hypothesis.
Probably Related	Follows a reasonable temporal sequence from the time of study drug administration; and/or Follows a known response pattern to the study drug.
Possibly Related	Follows a reasonable temporal sequence from the time of study drug administration; and/or Follows a known response pattern to the study drug; but could have been produced by other factors such as the patient's clinical state, therapeutic intervention, or concomitant therapy.
Unlikely Related	Does not follow a reasonable temporal sequence from the time of study drug administration; and Was likely produced by other factors such as the patient's clinical state, therapeutic intervention or concomitant therapy, but for which relationship cannot be definitely ruled out.
Not related	The adverse event can be determined with certainty to have no relationship to the study drug.

11.6 FOLLOW-UP OF ADVERSE EVENTS

Adverse events that have not resolved by the end of the safety follow-up period will be recorded as ongoing. However, subjects with a related AE of Grade ≥ 2 will be further followed (during Survival Follow-Up) until the resolution of the AE to Grade ≤ 1 or until beginning of a new anti-cancer treatment, whichever occurs first.

SAEs that have not resolved by the end of the safety follow-up period are followed until final outcome is known. If it is not possible to obtain a final outcome for a SAE (e.g., the subject is lost to follow up), the reason that a final outcome could not be obtained will be documented by the Investigator.

SAEs that occur after the safety follow-up (i.e., 30 days after the last dose of the study treatment) that are assessed by the Investigator to be related to study agent must be reported to the Drug Safety designee on the SAE worksheet.

11.7 REPORTING SERIOUS ADVERSE EVENTS TO THE RESEARCH ETHICS BOARD

All SAEs that are considered unexpected and related to the study agent will be reported by the Sponsor or designee as expedited (i.e., 15-Day) reports to the appropriate regulatory authorities AND to all participating Investigators. In addition, the Sponsor or designee follows all applicable local and national regulatory requirements regarding safety reporting. Each Investigator must also comply with the applicable regulatory requirements related to the reporting of SAEs to the Institutional Review Board/Ethics Committee (IRB/EC) responsible for reviewing the study at their site, as well as the regulatory authority(ies) (if applicable).

12. STATISTICAL ANALYSIS

Final statistical analyses (excluding interim analyses) will be performed once that last enrolled subject has completed 4 cycles of treatment or has progressed, whichever comes first, and that the database has been locked.

[redacted]

12.2 SAFETY LEAD-IN PERIOD

The assumptions to be applied in establishing the mTPI[2] methodology are:

- the maximum tolerated dose (MTD) is defined to have 0.30 probability of toxicity; and
- the acceptable variance around the MTD is ± 0.05 (i.e., the region of the MTD is 25% to 35% incidence of dose limiting toxicity (DLT)).

The mTPI model will determine the number of toxicities relative to subjects enrolled in the safety lead-in before the dose de-escalation decision is made. No dose escalation will be allowed. The number of subjects with DLTs observed relative to the number of subjects treated at a specific dose determines whether dose de-escalation is needed. The treatment will be considered acceptable if no more than 3 subjects experienced a DLT during the first cycle in the first 8 subjects treated and being part of the DLT Evaluable population. De-escalation to AB-16B5 9 mg/kg dose will be performed if more than 3 subjects experienced a DLT in the first 8 subjects treated. The next three subjects will then be evaluated at this lower dose. If 0 or 1 subject experienced a DLT during the first cycle in these 3 subjects, the AB-16B5 9 mg/kg dose will be considered acceptable. A final de-escalation of AB-16B5 to 6 mg/kg will be performed if more than 1 subject experienced a DLT at 9 mg/kg and the safety profile will be evaluated using the same process as described above.

For these purposes, a DLT will be defined as a Grade ≥ 3 non-hematologic toxicity occurring during Cycle 1 of therapy. In addition, the following hematologic toxicities will be considered as a DLT:

- Grade ≥ 4 neutropenia or thrombocytopenia > 7 days
- Grade ≥ 3 thrombocytopenia with bleeding
- Grade ≥ 3 febrile neutropenia

Toxicities that are clearly and incontrovertibly due to disease progression or to extraneous causes will <u>not</u> be considered DLTs. In addition, the following non-hematologic toxicities will <u>not</u> be considered DLTs:

- Grade 3 arthralgia or myalgia which returns to Grade ≤ 1 within < 7 days with appropriate supportive care
- Grade 3 nausea, vomiting or diarrhea which returns to Grade ≤ 1 within < 72 hours with appropriate supportive care
- Grade 3 fatigue lasting < 7 days
- Grade 3 electrolyte abnormalities that last less than 72 hours and are not associated with clinical symptoms

- Grade 3 amylase or lipase elevation which is not associated with symptoms or clinical manifestations of pancreatitis

12.3 DATA HANDLING

Listings of all subject data will be prepared. Data summaries will be presented in tabular and/or graphical format and summarized descriptively, where appropriate. Detailed analyses will be described in the SAP.

For all variables, only the observed data from subjects will be used in the statistical analyses; there is no plan to estimate missing data. Subjects without a valid clinical response assessment will be assigned a best overall response of not evaluable (NE). Data from subjects who are lost to follow-up or have missing observations before reaching an endpoint in any of the time-to-event analyses will be treated as censored with specific rules defined in the SAP.

12.4 ANALYSIS POPULATIONS

12.4.1 Clinical Activity Evaluable Population

The Clinical Activity Evaluable population will include all subjects who receive at least one dose of each study treatment drug (AB-16B5 and Docetaxel) and have at least one on-study disease assessment (post-dose) or develop early progression and discontinue study treatment prior to the first planned on-study disease assessment. Subjects who discontinue both study treatment drugs due to any other reason prior to their on-study disease assessment will not be included in the Clinical Activity Evaluable population.

This population will be used to evaluate futility rules as per PPD, to present tumor responses data and summary statistics.

12.4.2 mITT Population

The modified Intent-to-Treat (mITT) population will include subjects who receive at least one dose of each study treatment (AB-16B5 and Docetaxel).

This population will be used to present PFS and OS.

12.4.3 Safety Population

The Safety population is defined as all subjects who received at least one dose of any study treatment drug (i.e., AB-16B5 or Docetaxel). The Safety population will be used for all safety analyses.

12.4.4 DLT Evaluable Population

The DLT Evaluable population is defined as all subjects enrolled in the safety lead-in period who experienced a DLT during Cycle 1 or who completed one cycle of treatment (all 3 complete doses of AB-16B5 and 1 complete dose of Docetaxel). Subjects who are not evaluable for DLT will be

replaced. The DLT Evaluable population will be used to present the DLT AEs and for dose de-escalation decisions during the safety lead-in period.

12.4.5 PK Evaluable Population

The PK Evaluable population for the noncompartmental analysis is defined as all subjects who received AB-16B5 and have at least 3 measurable and adequately documented concentrations.

The PK Evaluable population for the population pharmacokinetic analysis is defined as all subjects who received AB-16B5 and have at least one adequately documented concentration.

12.4.6 Pharmacodynamic (PD) Evaluable Population

The PD Evaluable population will include all subjects who receive at least one dose of AB-16B5 and have at least one measurable biomarker.

12.5 EFFICACY ENDPOINTS DEFINITIONS AND ANALYSES

12.5.1 Objective Response Rate

Objective disease response will be categorized in accordance with RECIST 1.1.

Objective response rate (ORR) is defined as the percent of subjects documented to have a confirmed complete response (CR) or partial response (PR).

The primary endpoint of ORR will be tested using PPD. Descriptive statistics (frequency, percentage, and 95% CI) for ORR and best overall response (CR, PR, SD, PD, NE) will be presented.

12.5.2 Clinical Benefit Rate

Clinical benefit rate (CBR) is defined as the percentage of subjects documented to have a confirmed complete response (CR) or partial response (PR), or stable disease (SD) documented during at least 2 on-study assessments and including at least 10 weeks on study (i.e., allowance for 2-week window around Week 12 assessment).

Descriptive statistics (frequency, percentage, and 95% CI) for CBR will be presented.

12.5.3 Duration of Response

Duration of response (DOR) is defined as the time from date of the first documentation of objective tumor response (CR or PR) to the first documentation of objective progression of disease (PD) or to death due to any cause in the absence of documented PD. DOR will only be calculated for the subgroup of subjects achieving a confirmed CR or PR. The Kaplan Meier method will be used to estimate median DOR. Subjects with objective tumor response, and alive without PD at the end of the study will be censored at the date of their last tumor assessment. Other rules and time points for censoring for DOR will be specified in SAP.

12.5.4 Duration of Clinical Benefit

Duration of clinical benefit is defined as the time from date of the first documentation of clinical benefit to the first documentation of objective progression of disease (PD) or to death due to any cause in the absence of documented PD. Duration of clinical benefit will only be calculated for the subgroup of subjects achieving a clinical benefit. The Kaplan Meier method will be used to estimate median duration of clinical benefit. Subjects with clinical benefit, and alive without PD at the end of the study will be censored at the date of their last tumor assessment. Other rules and time points for censoring for duration of stable disease will be specified in SAP.

12.5.5 Duration of Stable Disease

Duration of stable disease is defined as the time from date of the first documentation of stable disease to the first documentation of objective progression of disease (PD) or to death due to any cause in the absence of documented PD. Duration of stable disease will only be calculated for the subgroup of subjects achieving a stable disease as their best overall response. The Kaplan Meier method will be used to estimate median duration of stable disease. Subjects with stable disease, and alive without PD at the end of the study will be censored at the date of their last tumor assessment. Other rules and time points for censoring for duration of stable disease will be specified in SAP.

12.5.6 Progression-Free Survival

Progression-free survival (PFS) is defined as the time from date of first study treatment to first PD or death due to any cause in the absence of documented PD. Censoring for the PFS endpoint will be assigned on the date of the last tumor assessment if no assessment of tumor progression is identified and the subject does not die while on study. For subjects in whom two or more sequential assessments are missed, followed by the finding of tumor progression, the PFS endpoint will be censored on the date of the last tumor assessment before the gap. Subjects lacking an evaluation of disease after first study treatment will have their PFS time censored on the date of first dose with duration of 1 day. Subjects who start a new anti-cancer therapy prior to documented PD will have the endpoint censored at the date of the last tumor assessment prior to the start of the new therapy. The Kaplan-Meier method will be used to obtain the estimate of median progression-free survival time.

12.5.7 Overall Survival

Overall survival (OS) is defined as the time from date of first study treatment to death due to any cause. The Kaplan-Meier method will be used to estimate the median OS and 1-year Survival Rate. The 95% CI of the 1-year survival rate will also be reported. Censoring for the survival endpoint will be assigned on the date of the last on study follow-up that the subject is reported to be alive.

[redacted]

12.5.9 Subgroup Analyses

There will be no subgroup analyses.

12.6 SAFETY DATA PRESENTATIONS AND SUMMARIES

12.6.1 Adverse Events

AEs will be classified using the medical dictionary for regulatory activities (MedDRA) classification system. Listings will include the verbatim term, Preferred Term (PT), and System Organ Class (SOC). The number of subjects with AEs and the incidence of AEs by SOC and PT will be summarized. AEs will be summarized by maximum intensity and relationship to study therapy. Separate summaries will be provided for AEs, SAEs, treatment-related AEs, treatment related SAEs, and other significant AEs (e.g., AEs leading to study discontinuation).

12.6.2 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization (WHO) medical dictionary; subjects who received these medications will be listed and summarized.

12.6.3 Clinical and Laboratory Assessments

Clinical and laboratory assessments include clinical laboratory tests (hematology, biochemistry, urinalysis and coagulation), vital signs, physical exams, ECOG, and 12 lead ECGs.

All clinical laboratory results will be listed by subject. Hematology, biochemistry and urinalysis will be summarized descriptively, which will include a display of change from baseline. Selected parameters will be presented in shift tables of baseline (from normal to abnormal, abnormal to normal, etc.). Laboratory values outside of the normal ranges will be identified.

Vital signs and ECG measurements will be listed for each subject at each available visit. For vital signs, descriptive statistics of observed values and changes from baseline will be summarized by treatment group.

ECOG will be presented in terms of number and percentage of subjects in each category, by visit.

12.6.4 Subject Demographics, Baseline Characteristics and Disposition

Demographic, baseline disease characteristics, medical history, primary disease history and prior systemic therapies/surgeries will be summarized and listed based on safety population. Subject

enrollment and disposition including reasons for study withdrawal and reasons for treatment discontinuation will be summarized.

12.6.5 Analysis of Study Treatment Dosing

Study treatment administration will be described in terms of the duration of exposure, total number of cycles administered, for each agent separately and for the combination, compliance, cumulative dose and reasons for the deviations from planned therapy.

12.7 OTHER STUDY ENDPOINTS

12.7.1 Pharmacokinetic Analysis

Noncompartmental analysis (NCA) of pharmacokinetic data will be conducted using standard approaches which will be defined in a separate analysis plan. If feasible, the peak concentration (C_{max}), area under the concentration time curve (AUC), clearance (CL), volume of distribution (Vz) and half-life will be reported. Summary statistics will be provided.

The pharmacokinetic data may also be evaluated using a population pharmacokinetics approach.

[redacted]

12.8 INTERIM ANALYSES

Interim safety evaluation will be conducted once 8 evaluable subjects (i.e., part of the DLT-evaluable population) are obtained.

Interim futility evaluations will be conducted once 10 evaluable subjects (i.e., part of the Clinical Activity Evaluable population) are obtained and every 8 evaluable subjects thereafter.

13. STUDY ADMINISTRATION

13.1 INFORMED CONSENT

A copy of the proposed informed consent document must be submitted to the Sponsor or designee for review and comment prior to submission to the reviewing IRB/EC. The consent form must be approved by the IRB/EC and contain all elements required by national, state, local, and institutional regulations or requirements.

It is the responsibility of the Investigator to provide each subject with full and adequate verbal and written information using the IRB/EC approved informed consent document(s), including the objective and procedures of the study and the possible risks involved before inclusion in the study.

Each subject must voluntarily provide written informed consent (including consent for the use and disclosure of research-related health information). The consent must be obtained prior to performing any study-related procedures that are not part of normal subject care, including screening and changes in medications including any washout of medications. A copy of the signed informed consent must be given to the study subject.

13.2 RESEARCH ETHIC BOARD REVIEW AND APPROVAL

The Investigator or Sponsor shall assure that the IRB/EC, constituted in accordance with the ICH Guideline for Good Clinical Practice (GCP), will provide initial and continuing review of the study. Prior to shipment of the study treatment and enrollment of study subjects, documented IRB/REC approval of the protocol, informed consent form must be obtained and provided to the Sponsor or designee.

The IRB/EC must also be informed of all protocol amendments prior to implementation. The Investigator must provide reports of any change in research activity (i.e. the completion, termination, or discontinuation of a study) to the IRB/EC.

13.3 PROTOCOL COMPLIANCE

Except for a change that is intended to eliminate an apparent immediate hazard to a study subject, the protocol shall be conducted as described. Any such change must be reported immediately to the Sponsor and to the IRB/EC.

13.4 PROTOCOL REVISIONS

Protocol amendments will be prepared and approved by the Sponsor. All protocol amendments will be signed by the Investigator and submitted to the IRB/EC for review prior to implementation. Documentation of IRB/EC approval must be forwarded to the Sponsor or designee. If an amendment significantly alters the study design, increases potential risk to the subject or otherwise affects statements in the informed consent form, the informed consent form must be revised accordingly and submitted to the IRB/EC for review and approval. The approved consent form must be used to obtain informed consent from new subjects prior to enrollment and must be used to obtain informed consent from subjects already enrolled if they are affected by the amendment.

13.5 DATA ENTRY INTO eCRF

Study-specific eCRFs will be made available to the site. Study data, contained in source documentation, will be entered into the eCRFs for all subjects enrolled in the study. All pertinent data records are to be submitted to the sponsor during and/or at completion or termination of the study.

The Investigator agrees that qualified representatives of the sponsor and regulatory agencies will have the right, both during and after this study, to conduct inspections and to audit and review medical records pertinent to the clinical study as permitted by the regulations. Subjects will not be

identified by name in any reports stemming from the study, and confidentiality of information in medical records will be preserved. The confidentiality of the subject will be maintained unless disclosure is required by regulations. Accordingly, the following statement (or similar statement) that permits the release of the subject's medical records will be included in the informed consent document: *Representatives of regulatory agencies, IRB/EC, the sponsor, and the subject's personal physician may review the subject medical records and all information related to this study as permitted by law. Subject identity will remain confidential unless disclosure is required by law.*

13.6 STUDY MONITORING

The Sponsor or designee will monitor the study. Study monitors representing the Sponsor will routinely visit study sites throughout the trial.

Routine monitoring visits will be conducted to:

- Assure compliance with the study protocol;
- Verify that the informed consent process was conducted before initiation of any screening procedures that are performed solely for the purpose of determining eligibility for the study and prior to the provision of study medication;
- Verify that the protocol, protocol amendments, and safety information are submitted to the IRBs/EC and approved by the IRBs/EC in a timely manner;
- Review the eCRFs and source documents to ensure that reported study data are accurate, complete, and verifiable from source documents;
- Verify that the investigational products are stored properly and under the proper conditions, that they are in sufficient supply, and that receipt, use, and return of investigational products at the study centers are controlled and documented adequately;
- Verify that the Investigator and study center personnel remain adequately qualified throughout the study; and
- Verify that the research facilities, including laboratories and equipment, are maintained adequately to safely and properly conduct the study.

Auditors representing the Sponsor may also evaluate the study and its monitors. For these purposes, the Investigator will make eCRFs and source documents available when requested.

In addition, the study may be evaluated by representatives of the regulatory authorities, who will also be allowed access to study documents. The Investigator should promptly notify the Sponsor of any audits they have scheduled with any regulatory authority.

13.7 RETENTION OF RECORDS

The Investigator shall retain all records and source documents pertaining to the study, including any films, tracings, computer discs or tapes. They will be retained for the longer of the maximum

period required by the country and institution in which the study is conducted, or the period specified by the Sponsor at the time the study is completed, terminated or discontinued.

If the Investigator leaves the institution, the records shall be transferred to an appropriate designee who accepts the responsibility for record retention. Notice of such transfer shall be documented in writing and provided to the Sponsor.

13.8 FINANCIAL DISCLOSURE

The Investigator will provide the Sponsor sufficient and accurate information on financial interests (proprietary or equity interests, payments exclusive of clinical trial costs) to allow complete disclosure to regulatory authorities. The Investigator shall promptly update this information if any relevant changes occur during the course of the investigation and for a period of 1 year following study completion.

13.9 STUDY OR STUDY SITE TERMINATION

If the Sponsor, the Investigator, IRB/EC or a regulatory authority discovers conditions arising during the study that indicate that the study should be halted or that the study center should be terminated, this action may be taken after appropriate consultation between the Sponsor and the Investigator. Conditions that may warrant termination of the study include, but are not limited to, the following:

- The discovery of an unexpected, serious, or unacceptable risk to the subjects enrolled in the study.
- A decision on the part of the Sponsor to suspend or discontinue testing, evaluation, or development of the product.

The study site may warrant termination under the following conditions:

- Failure of the Investigator to enroll subjects into the study at an acceptable rate.
- Failure of the Investigator to comply with pertinent regulatory authority regulations.
- Submission of knowingly false information from the research facility to the Sponsor, study monitor, or the regulatory authority.
- Insufficient adherence to protocol requirements.

13.10 CLINICAL STUDY REPORT

The final CSR will be issued when all subjects enrolled in the study will have ended their participation in the trial.

14. REFERENCES