UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q/A
(Amendment No. 1)

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2011

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number 001-14895

AVI BIOPHARMA, INC.
(Exact name of registrant as specified in its charter)

Oregon	**93-0797222**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3450 Monte Villa Parkway, Suite 101, Bothell, Washington	**98021**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (425) 354-5038

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act (Check one):

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller Reporting Company	☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Common Stock with $0.0001 par value	**135,743,120**
(Class)	(Outstanding as of October 26, 2011)

Explanatory Note

We are filing this Amendment No. 1 to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2011 (the "Amendment") only to re-file Exhibit 10.3 in response to comments we received from the Securities and Exchange Commission on a confidential treatment request we made for certain portions of the exhibit in our original Form 10-Q. The re-filed exhibit discloses portions that had previously been redacted pursuant to our request for confidential treatment.

This Amendment does not reflect events occurring after the filing of our original Form 10-Q or modify or update those disclosures affected by subsequent events. No other modifications or changes have been made to our Form 10-Q for the quarter ended September 30, 2011 as originally filed or the exhibits filed therewith.

PART II - OTHER INFORMATION

Item 6. Exhibits.

Exhibit No	Exhibit Description	Incorporated by Reference to Filings Indicated				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.3†	Modification No. P00005 to Contract Number W9113M-10-C-0056 between U.S. Army Space and Missile Defense Command and AVI BioPharma, Inc. effective August 15, 2011.					X
31.1	Certification of the Company's President and Chief Executive Officer, Christopher Garabedian, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of the Company's Vice President, Finance, Michael Jacobsen, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X

† Portions of this exhibit are omitted and were filed separately with the Securities and Exchange Commission pursuant to an application requesting confidential treatment.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: February 15, 2012

AVI BIOPHARMA, INC.

By: /s/ CHRISTOPHER GARABEDIAN
Christopher Garabedian
President and Chief Executive Officer

EXHIBIT INDEX

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Exhibit 10.3

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT	1. CONTRACT ID CODE V	PAGE OF PAGES 1 | 3

2. AMENDMENT/MODIFICATION NO.	3. EFFECTIVE DATE	4. REQUISITION/PURCHASE REQ. NO.	5. PROJECT NO. *(If applicable)*
P00005	08/15/2011	see schedule	

6. ISSUED BY	CODE	W911QY	7. ADMINISTERED BY *(If other than Item 6)*	CODE	S4801A
NATICK CONTRACTING DIVISION 64 Thomas Johnson Drive Frederick MD 21702-4300			DCMA DCMA-SEATTLE CORPORATE CAMPUS EAST III 3009 112TH AVE. NE STE200 BELLEVUE WA 98004-8019		

8. NAME AND ADDRESS OF CONTRACTOR *(No., street, county, State and ZIP Code)*	(X)	9A. AMENDMENT OF SOLICITATION NO.
AVI BIOPHARMA INC 4575 SW RESEARCH WAY STE 200 CORVALLIS OR 97333-1299	☐	9B. DATED *(SEE ITEM 11)*
	☒	10A. MODIFICATION OF CONTRACT/ORDER NO. W9113M-10-C-0056
CODE 49WU1 FACILITY CODE		10B. Dated *(SEE ITEM 13)* Jul 14, 2010

11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS

☐ The above numbered solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers ☐ is extended, ☐ is not extended.

Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods:

(a) By completing items 8 and 15, and returning copies of the amendment; (b) By acknowledging receipt of this amendment on each copy of the offer submitted;

or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment your desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.

12. ACCOUNTING AND APPROPRIATION DATA *(If required)*

See SCHEDULE

13. THIS ITEM ONLY APPLIES TO MODIFICATION OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.

CHECK ONE	
☐	A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: *(Specify authority)* THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.
☐	B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES *(such as changes in paying office, appropriation date, etc.)* SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(b).
☒	C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF: Mutual Agreement of Both Parties
☒	D. OTHER *(Specify type of modification and authority)*

E. IMPORTANT: Contractor ☐ is not, ☒ is required to sign this document and return 1 copies to the issuing office.

14. DESCRIPTION OF AMENDMENT/MODIFICATION (*Organized by UCF section headings, including solicitation/contract subject matter where feasible.*)

See Attached Summary of Changes.

Except as provided herein, all terms and conditions of the document referenced in Item 9A or 10A, as heretofore changed, remains unchanged and in full force and effect.

15A. NAME AND TITLE OF SIGNER *(Type or print)*	16A. NAME AND TITLE OF CONTRACTING OFFICER *(Type or print)*
Chris Garabedian President and CEO	Sandra J. O'Connell Contracting Officer

15B. CONTRACTOR/OPERATOR	15C. DATE SIGNED	16B. UNITED STATES OF AMERICA	16C. DATE SIGNED
/s/ Chris Garabedian *(Signature of person authorized to sign)*	9/23/11	/s/ Sandra J. O'Connell *(Signature of Contracting Officer)*	9/26/11

NSN 7540-01-152-8070 STANDARD FORM 30 (Rev. 10-83)
Previous edition unusable Prescribed by GSA FAR (48 CFR) 53.243

† DESIGNATES PORTIONS OF THIS DOCUMENT THAT HAVE BEEN OMITTED PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT FILED SEPARATELY WITH THE COMMISSION.

SECTION SF 30 BLOCK 14 CONTINUATION PAGE

SUMMARY OF CHANGES

A. The purpose of this modification is to move studies/tasks originally planned in Option CLINs 0002 and 0006 into CLINs 0001 and 0005 thereby affecting the total cost and schedule of this contract as shown below.

1. SECTION A – SOLICITATION/CONTRACT FORM

The total cost of this contract was increased by $46,142,707.00 from $80,396,827.37 to $126,539,534.37.

2. SECTION B – SUPPLIES OR SERVICES AND PRICES

CLIN 0001

The target cost has increased by $[†] from $[†] to $[†].
The target profit/fee has increased by $[†] from $[†] to $[†].
The minimum profit fee has increased by $[†] from $[†] to $[†].
The maximum profit fee has increased by $[†] from $[†] to $[†].
The total cost of this line item has increased by $[†] from $[†] to $[†].

CLIN 0002

The target cost has decreased by $[†] from $[†] to $[†].
The target profit/fee has decreased by $[†] from $[†] to $[†].
The minimum profit fee has decreased by $[†] from $[†] to $[†].
The maximum profit fee has decreased by $[†] from $[†] to $[†].
The total cost of this line item has decreased by $[†] from $[†] to $[†].

CLIN 0005

The target cost has increased by $[†] from $[†] to $[†].
The target profit/fee has increased by $[†] from $[†] to $[†].
The minimum profit fee has increased by $[†] from $[†] to $[†].
The maximum profit fee has increased by $[†] from $[†] to $[†].
The total cost of this line item has increased by $[†] from $[†] to $[†].

CLIN 0006

The target cost has decreased by $[†] from $[†] to $[†].
The target profit/fee has decreased by $[†] from $[†] to $[†].
The minimum profit fee has decreased by $[†] from $[†] to $[†].
The maximum profit fee has decreased by $[†] from $[†] to $[†].
The total cost of this line item has decreased by $[†] from $[†] to $[†].

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3. SECTION F – DELIVERIES OR PERFORMANCE

The following Delivery Schedule item for CLIN 0001 has been changed from:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
25-MAR-2012		N/A FOB: Destination	

To:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
18-APR-2013		N/A FOB: Destination	

The following Delivery Schedule item for CLIN 0005 has been changed from:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
01-APR-2012		N/A FOB: Destination	

To:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
10-MAY-2013		N/A FOB: Destination	

4. SECTION J – LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

Attachment No. 1 Contractor's Statement of Work – Ebola Virus, Dated 3/11/10 and Attachment No. 2 Contractor's Statement of Work – Marburg Virus, Dated 3/11/10 are replaced in their entirety with the Attachments to this modification.

B. An Integrated Baseline Review (IBR) will be held within 3 months of the date of this modification. At that time the Performance Measurement Baseline (PMB) will be approved by the Government for the changed efforts of CLINs 0001; 0002, 0005 and 0006. A modification will be executed upon acceptance of the PMB, and will incorporate any approved changes to the budget that are required.

C. As a result of this modification all other terms and conditions of this contract are unchanged and remain in full force and effect.

(End of Summary of Changes)

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Appendix B: Revised Statement of Work

3.0 CONTRACT

AVI BioPharma (AVI) Statement of Work for AVI-6002 as an effective therapeutic for ebolavirus:

3.2 CLIN0001 Technology Development (Part 1): AVI will deliver the developmental therapeutic end item that has completed [†] clinical trials, with all the associated preclinical and regulatory requirements sufficient and in place to support its delivery. This will comprise all those activities necessary for our candidate drug product to complete the US GOVERNMENT (USG) Statement of Objectives for CLIN0001. We will complete the planning (including assessment and mitigation of risk) for manufacturing the drug supply, and execute process development to enable scale up from the current [†] batch GLP material, through a [†] batch cGMP engineering development scale, in anticipation of an ultimate [†] modular manufacturing scale; includes analytical methods development and validation ([†], drug substance) and method qualification (drug product), and development of specifications for lot release.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Drug product on which [†] clinical trials have been completed.

3.2.2 [†] Process Development and Qualification: AVI will prepare drug substance for use in subsequent [†] studies (includes the use of previously manufactured components outside this RFP to prepare drug substance). The [†] development program will improve process reproducibility and prepare for manufacturing at larger scales. AVI will investigate several steps that have shown variability [†], and examine steps that have challenges in scale-up [†]. The overall goal of drug substance development is to design a [†] process that is highly reproducible, and that can be demonstrated at [†] scale, and usable in the final manufacturing [†] scale. [†]. A stable, [†] form of the drug substance will be produced.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Design scalable processes for [†] and drug substance.

3.2.2.1 [†] Process Development and Qualification: The [†] development program is aimed at improving reproducibility and scalability, and ensuring the quality of the product. The overall goal is to design [†] process that is highly reproducible and easily scalable.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Finalization of a highly reproducible and easily scalable [†] process in preparation for manufacturing at larger scales.

3.2.2.1.1 Synthesis and Characterization of Authentics: This project will help ensure a consistent quality of product. [†]. These authentics will be used as markers in the analytical method validation to check the resolution of the methods.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Preparation of authentic impurity markers

3.2.2.1.2 [†] Process Development: The [†] development program is aimed at improving reproducibility and scalability. It will investigate several steps that have shown [†]. The overall goal is to design a [†] process that is highly reproducible and easily scalable.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Improvement of specific steps and finalization of a highly reproducible and easily scalable [†] process.

3.2.2.1.3 Project Management, Operations and Oversight: Project management will oversee the CROs that are performing [†] process development and will also manage the in-house development effort

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.2.2 Drug Substance [†] Process Development: The drug substance [†] process development program will involve optimization of the [†] components of the manufacturing process. The overall goal is to design a highly reproducible and scalable [†] drug substance manufacturing process that can be demonstrated at an [†] and is usable in the final manufacturing [†] scale.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Demonstration of a reproducible and scalable manufacturing process for drug substance.

3.2.2.2.1 Drug Substance [†] Process Development: Development activities are to include optimization of [†] to produce a scalable synthesis process as well as optimization of current [†] process to increase efficiency of [†]. Investigation of alternative [†] methods [†] will also be conducted.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Optimization of the synthesis and [†] components of the manufacturing process.

3.2.2.2.2 Project Management, Operations and Oversight: This element entails oversight and guidance of the development activities, as well as management of technical personnel.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.3 Manufacturing for Nonclinical Studies:** [†] production will occur at [†], and will supply all the [†] needed for CLIN0001 drug substance manufacture, plus a contingency plan for any drug substance batch needing to be repeated (this is essential to ensure concordance with the timeline). Any

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excess [†] will be used during the scale up in CLIN0002. The current [†] drug substance process will be transferred to a contract manufacturing organization (CMO) accomplished in the [†] manufacture of oligomeric therapeutic drugs. The CMO will perform scaling of process to [†], plus process development and Reduction to Practice (RtP) run(s). Material for toxicology studies will be made.

** Drug Product for the [†] clinical trial has already been manufactured and is currently stored awaiting final preparations for the start of the study.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Produce drug substance for [†] studies using [†] scale drug substance process.

3.2.3.1 Manufacture [†]: This production is planned to occur at [†]. It will produce all the [†] needed for CLIN0001 drug substance manufacture plus a contingency if a drug substance batch needs to be repeated. Any excess [†] will be used during the scale up in CLIN0002.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Timely supply of [†] to support CLIN0001 drug substance development and manufacture.

3.2.3.1.1 Contract Negotiation, Material Acquisition: Finalize and sign contracts for production. Order long lead time and custom reagents to support upcoming campaign.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Contract and materials in place for [†] manufacture.

3.2.3.1.2 Manufacture [†]: Produce all the [†] needed for CLIN0001 drug substance development and manufacture.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Timely supply of [†] to support CLIN0001 drug substance development and manufacture.

3.2.3.1.3 Quality Audits and Review: Quality audits are managed by the Director of QA and scheduled in accordance with the Audit Master Schedule. Automatic audit reminders are issued by the EDMS. Auditors schedule travel to and from audits, write audit reports, provide lists of findings and make recommendations. The Director of QA oversees all operational aspects of audits, procedures connected with audits and audit reports. Audit findings, recommendations and responses are reviewed by the Director of QA, the VP of Regulatory Affairs and QA. Non-compliance issues are brought to the attention of the Chief Executive Officer (CEO), personally, by the Director of QA on a biweekly basis. In addition, a QA Unit and Compliance Report is written monthly by the Director of QA and presented to the CEO in a 1:1 meeting. Functional management and staffing of the QA Unit is the responsibility of, and managed by, the VP of Regulatory Affairs and QA.

Quality Audits include non-cGMP, non-GLP, cGMP or GLP audits, depending on the process step and may include audits of non-regulated facilities (non-cGMP and non-GLP facilities) or audits of facilities

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that are required to comply with cGMP or GLP. These are Direct Impact audits of Contract Manufacturing Organizations (CMOs), quality control testing, storage and distribution facilities connected with the manufacture of [†] and activated tails. Audit documentation includes a list of questions directly suited to the service provided by the CMO and an ICH Q7-compliant audit checklist. All CMOs must be audited and approved by QA and, when applicable, readiness for Pre-Approval Inspection (PAI) by the FDA or other regulatory agency is evaluated at an appropriate time during an audit. Audit records have limited, controlled review access for authorized departmental and senior management staff, and are reviewed through and archived using the EDMS.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: QA approved CMO (vendor) and release of manufactured [†] for AVI-6002 program. Audit report completed and satisfactory resolution of responses to findings for CMO providing [†]. Lot release of [†] for drug substance manufacturing program in accordance with QA-approved specifications using analytical methods.

3.2.3.1.4 Project Management, Operations and Oversight: Project management will oversee the CMO that is doing the CLIN0001 production.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.3.2 Manufacture Drug Substance: Select CMO experienced in [†] synthesis of [†] drugs. Tech transfer of [†] scale process for drug substance; scale-up of process to [†], process development and RtP run(s); determine stable [†] form for drug substance.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Achieve [†] scale drug substance process and produce material for [†] studies.

3.2.3.2.1 Select, Contract, and Audit CMO: CMOs capable of performing [†] synthesis have been reviewed for suitability for the API manufacture, [†], and isolation. Site visits will be performed followed by quality audits, contract negotiations, technical transfer, and Quality agreement execution.

Period of Work: Approximately [†] days from time of award (e.g. [†])

Deliverable: Selection and completion of contracts with a suitable CMO for API manufacture.

3.2.3.2.2 Manufacturing Tech Transfer at [†]: Production will be introduced at the current [†] scale to allow comparability of previous lots and to transfer knowledge to the new CMO. Each API will be made and purified at this scale with the objective being to produce material suitable for toxicological studies.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Demonstration of successful tech transfer of current [†] sale and production of material suitable for [†] studies

3.2.3.2.3 Process Development, Reduction to Practice at [†]: After the tech transfer campaigns, the process size will be adapted to an approximately [†] scale as part of normal development in order to produce more material suitable for [†] studies. At this point process changes may be introduced to make the process more efficient as long as the impurity profiles remain unchanged. The batch will be run cGMP in order to supply material for the QTc clinical study and pivotal animal study in CLIN0002.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Demonstration of scalability of manufacturing process to [†] scale by successful completion of RtP run(s). Holding the API until needed for fill finish. Ship material for formulation development to precede the fill/finish in CLIN0002. Supply C of A.

3.2.3.2.4 Project Management, Operations and Oversight: As part of the normal course of outsourcing production, regular team meetings will be held and updates provided. Production oversight from site visits and data review will be shared and discussed. Regular conference calls with the CMO will be established to review progress and results.

Period of Work: Approximately [†] days from time of award (e.g. [†])

Deliverable: Plan, monitor, and report overall delivery of milestones and budget

3.2.4 Develop and Validate Analytical Assays and Lot Release Specifications: Existing analytical methods will be refined and validated for each [†]. Methods for drug substance will be developed and validated to meet characterization criteria set with the FDA for release. For the drug product assays, development will utilize synergies with drug substance methods to reduce time and cost of method qualification. For both drug substance and drug product, AVI will qualify vendors, facilities and conduct audits.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Validated assays for [†] and drug substance, qualification of the drug product assays, and development of lot release specifications for [†], drug substance and drug product.

3.2.4.1 [†] **Analytical Method Development and Validation:** Existing analytical methods will be refined and validated for each [†].

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited report for validated analytical methods for each [†].

3.2.4.1.1 Method Development and Validation: Methods confirming process consistency will be developed by a qualified subcontractor. Methods for assay and impurity profile will be validated to established criteria for cGMP starting materials.

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Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited report for validated analytical methods for each [†].

3.2.4.1.2 Identify Impurities above ID Threshold: Process-critical impurities will be synthesized and included in the validation process. Markers for known impurities will be synthesized as part of the impurity profile. Chromatograms of historic lots will be generated using the refined analytical methods. A team of chemists will work on identifying and synthesizing all impurities that occur [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Identification and preparation of markers for all impurities that occur above the [†].

3.2.4.1.3 Develop (Assess and Refine) Lot Release Specifications: To ensure consistent quality, a team will assess and refine all the [†] lot release specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Preparation of a lot release specification for each [†].

3.2.4.1.4 cGMP Audits: See section 3.2.3.1.3 Quality Audits and Review for general description of Quality Audits. cGMP audits are performed by experienced auditors for the Contract Manufacturing Organizations (CMOs), quality control testing and storage and distribution facilities. Audits employ a checklist approach, based on regulatory requirements and ICH Q7 guidelines, which are customized to comply with requirements for each subcontractor site and circumstance. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of cGMP and GLP subcontractors is also evaluated. Under the Quality System, batch release specifications, test methods and quality control test results, protocols for stability studies and analytical methods and study reports or data are reviewed for compliance with regulations and guidelines and approved by the Director of QA

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audit report completed and satisfactory resolution of responses to findings by subcontract laboratories testing [†] for drug substance for subsequent clinical use.

3.2.4.1.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.4.2 Drug Substance Analytical Method Development and Validation: Drug substance analytical methods will be developed and validated to meet characterization criteria set forth by regulatory agency for release. Impurities will be isolated and identified. Subcontractors will be qualified, and audits performed, by AVI QA Unit.

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Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited report for validated analytical methods for drug substance release.

3.2.4.2.1 Method Development and Validation: Methods, compliant with regulatory expectations, will be developed for impurity profile, assay, identity and description. Method validation will be performed by qualified vendor.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Methods for impurity profile, assay, identity and description, validated and audited report as appropriate.

3.2.4.2.2 Identify Impurities above [†]: Impurities will be identified and the identity verified by synthesis of authentic compounds. Detection level of impurities will be established.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Establish identity and detection levels of impurities.

3.2.4.2.3 Develop (Assess and Refine) Lot Release Specifications: Release specifications will be established that ensure consistency between production lots. RTP batches will be used to refine release specifications and assess the analytical method capability to meet the specification threshold according to ICH Q6A recommendations. Director of QA participates in review and approval of specifications that are compliant with cGMP and compendial requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: cGMP-compliant lot release specifications are approved for drug substance for subsequent clinical use.

3.2.4.2.4 Quality Audits and review: Documentation for drug substance (DS) analytical method development and validation will be reviewed by QA for compliance with regulatory requirements. See section 3.2.3.1.3 Quality Audits and Review and section 3.2.4.1.4 cGMP Audits. Audits occur, reports are completed and satisfactory responses are received to audit findings. Director of QA reviews and approves validation protocols and validation reports for the analytical methods.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audits occur, audit reports are completed audit findings are resolved and validated analytical tests and methods are approved for drug substance.

3.2.4.2.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.2.4.3 Drug Product (DP) Analytical Method Development and Qualification: Drug product analytical method development and qualification will characterize phosphate buffered saline filled drug product. Method development will utilize synergies with drug substance methods to reduce time and cost of method qualification. Includes subcontractor qualification and audits by AVI QA Unit.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Qualified analytical test methods (validated assay method) that comply with the FDA's quality and regulatory requirements for release of drug product.

3.2.4.3.1 Method Development and Qualification: Methods, compliant with regulatory expectations, will be developed for impurity profile, assay, identity, and description. Method qualification will be performed by qualified vendor. A contract analytical development laboratory will be chosen, and methods for drug product analysis and release will be developed that comply with the FDA's quality and regulatory requirements.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited reports for qualified methods for impurity profile, identity, and description and validated method for assay.

3.2.4.3.2 Identify Impurities above ID Threshold: Impurities will be identified and the identity verified by synthesis of authentic compounds. Detection level of impurities will be established.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Establish identity and detection levels of impurities

3.2.4.3.3 Develop (Assess and Refine) Lot Release Specifications: Release specifications will be established that ensure consistency between production lots. RTP batches will be used to refine release specifications and assess the analytical method capability to meet the specification threshold according to ICH Q6A recommendations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Lot release specification in compliance with the FDA's quality and regulatory requirements for drug product for subsequent clinical use.

3.2.4.3.4 cGMP Audits: Documentation for drug product (DP) analytical method development and validation will be reviewed by QA for compliance with regulatory requirements. See section 3.2.4.1.4 above. Audit occurs, report completed and satisfactory resolution of responses to findings by subcontract testing laboratories developing analytical methods and testing drug product for subsequent clinical use. Lot release will occur using QA-approved validated analytical methods and specifications compliant with compendia and other regulatory requirement.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Completed and QA reviewed validation reports. Audit report completed and satisfactory resolution of responses to findings by subcontract testing laboratories. Lot release tests and specifications that comply with the FDA's quality and regulatory requirements are approved by the Director of QA.

3.2.4.3.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.5 [†]: AVI will conduct [†] studies [†]. A new assay will be used for the determination of drug levels in biological matrices, and each component of the study drug will be assayed independently. The method will be validated (GLP) in plasma as is required for study protocols for pharmacokinetic analysis. An existing [†] will be transferred and validated (GLP) for the analysis of dosing solutions, over a [†]. The single dose [†] will evaluate the effect of a single dose on target organs observed. Quality Audits will be conducted on the contract research organization (CRO) and the audit records maintained by the AVI EDMS.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Completed GLP-compliant non-clinical toxicology study reports for studies in [†], including [†] reports.

3.2.5.1 [†] Method Validation: Feasibility studies have proven a [†] method acceptable for the determination of drug levels in biological matrices. Each component of the study drug is assayed independently. The method will be validated (GLP) in matrices corresponding to samples specified by study protocols for pharmacokinetic analysis [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on validated [†] method for detection of drug levels in biological matrices.

3.2.5.2 Dose Formulation Analytical Method Evaluation and Validation: An existing [†] method will be transferred and validated (GLP) for the analysis of dosing solutions. The method will be validated over a concentration range suitable for determination of concentration, homogeneity, and stability of the dose formulations for the non-clinical toxicology studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on validated method for concentration of drug levels.

3.2.5.3 [†]: The single dose [†] study will evaluate the effect of a [†]. The results will have an impact on the dosages and escalation in the [†] trial. This study requires validation of the analytical method.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.4 [†]: This study provides supportive data for the repeat dose study [†] that has been completed. Allow correlation of observed effects with exposure.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.5 [†]: In vitro study to assess the effects of the test article on [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.6 [†]: To investigate the actions of the test article/vehicle on action potential [†] methods. This study will identify potential risk of [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.7 [†] with Long Recovery: [†]. This study will determine [†] in multidose clinical trial

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] Study with Long Recovery.

3.2.5.8 cGLP Audits: Quality Audits conducted in this arena are Direct Impact audits of our Contract Research Organizations (CRO). Audits include a list of questions directly suited to the CRO and a GLP/cGMP [†] checklist. All CROs (through audits) are approved (or rejected) by QA and audit records are maintained by the AVI EDMS. See section 3.2.3.1.3 for general description of Quality Audits. Audits of [†] facilities, [†] laboratories, and related study data will be conducted by experienced auditors from the Quality Unit. Audits employ a checklist approach, based on regulatory requirements (21 CFR Part 58 for GLP compliance) and ICH guidelines. The checklists are customized to comply with requirements applicable for each subcontractor facility and type of testing. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of GLP subcontractors is also evaluated.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit report completed and acceptable responses to findings received from subcontract [†] facilities and [†] laboratories testing AVI-6002 for [†]. GLP studies will occur using QA-approved protocols that meet regulatory and IUCAC and USG requirements and validated [†] methods are used.

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3.2.5.9 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.6 Pilot [†] Studies: [†].

** [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete [†] studies.

3.2.6.1 [†]: [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and receive report for single vs combination agent AVI-6002 study.

3.2.6.2 GLP Audits: Quality Audits conducted in this arena are Direct Impact audits of our Contract Research Organizations (CRO). Audits include a list of questions directly suited to the CRO and a GLP/GMP (animal) checklist. All CROs (through audits) are approved (or rejected) by QA and audit records are maintained by the AVI EDMS. See section 3.2.5.8 above. See section 3.2.3.1.3 for general description of Quality Audits. Audits of animal testing facilities, bioanalytical laboratories, and related study data will be conducted by experienced auditors from the Quality Unit. Audits employ a checklist approach, based on regulatory requirements (21 CFR Part 58 for GLP compliance) and ICH guidelines. the checklists are customized to comply with requirements applicable for each subcontractor facility and type of testing. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of GLP subcontractors is also evaluated.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audit and report completed and satisfactory responses to audit findings received from [†] facilities and [†] testing drug product for nonclinical studies. GLP studies will occur using QA-approved protocols that meet regulatory and IUCAC and USG requirements and validated bioanalytical methods are used

3.2.6.3 Project Management, Operations and Oversight: The antiviral team will meet regularly to review the protocol, monitor progress of the studies and evaluate observations. In addition, weekly conference calls with [†] will provide coordination of effort and timing.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.2.7 Contract Program Management:** AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall study are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

** Work will continue during period [†] on this program – namely [†] and regulatory to prepare for [†] clinical study. Program management will be required to oversee those tasks.

Period of Work: Concurrent with all CLIN0001 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.2.7.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0001 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3.2.7.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Concurrent with all CLIN0001 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.2.7.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0001 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance

3.2.7.4 EDMS Installation, Validation, Implementation, Training and QA: AVI will implement enhancements to the Quality Systems Approach already in place, including installation of a secure 21CFR Part 11 compliant EDMS and preparation for electronic document submission to the FDA. AVI will train all pertinent staff on EDMS and Quality Assurance.

Period of Work: Concurrent with all CLIN0001 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: EDMS system will have been selected, installed and fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.3 CLIN0001 Technology Development – [†] Clinical Study (Part 2): Using the currently filed IND, and [†] data obtained subsequently, AVI will establish agreement with the FDA for the acceptable protocol** [†], such as [†] review and approval. AVI will conduct and report the [†] clinical study in healthy [†].

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** Discussions with the FDA are planned for [†] which will cover the [†] and additional input to the proposed [†] study may be requested.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Final study report for [†] clinical study agreed upon by the government.

3.3.1 Support [†] Submission: An [†] cannot be granted until the appropriate legislative order has been given by Congress, however, AVI will submit a Request for Consideration for an [†] and briefing document (per Section 564(c) of the FD&C Act), amendments under Project Bioshield Act of 2004, and draft FDA Guideline of June 2005. The Request for Consideration will contain data from all available research and nonclinical studies together with draft protocol synopses for the [†] studies and the first clinical study. The FDA will be asked to provide advice on the additional requirements to achieve an [†].

As requested by the FDA in the meeting, AVI will continue to submit additional scientific, [†] and [†] study data in final study reports as [†] when the final reports are available with the intention of fulfilling all requirements for an [†] before such use is required.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Letter to the FDA requesting a meeting to discuss the Request for Consideration as an [†] and Briefing Document submitted as an [†]. In addition, after the meeting with the FDA the company's notes of the meeting with the FDA will be submitted as an [†].

3.3.1.1 Support [†] Submission, Meeting with FDA and USG: AVI's regulatory affairs staff will prepare the Meeting Request Letter and Briefing Document for the Request for Consideration as an [†] Meeting with the FDA and submit them as [†]. After the Meeting with the FDA, AVI's regulatory affairs staff will prepare notes of the meeting and submit them as an [†]. The Request for Consideration as an [†] submissions will be planned, prepared and managed by AVI's regulatory affairs staff, using FDA compliant electronic templates, e-publishing techniques and the EDMS. Meeting arrangements and follow-up Meeting Minutes will also be prepared and managed by RA. Oversight will be provided by AVI's senior management.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Letter to the FDA requesting a meeting to discuss a Request for Consideration as an [†] and Briefing Document submitted as an [†]. After the meeting with the FDA the company's notes of the [†] with the FDA will be submitted as an [†].

3.3.1.2 Project Management, Operations and Oversight: Consideration as an [†] request managed by AVI regulatory affairs, using FDA compliant electronic templates, electronic document management and e-submission. Meeting arrangements and follow-up meeting minutes also managed by RA. Oversight is provided by AVI's senior management.

Period of Work: Approximately [†] days from meeting date being offered with FDA (e.g. [†]).

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Deliverable: Plan, monitor, and report overall delivery of milestones to timeline and budget.

3.3.2 [†] Clinical Study: The [†] will be conducted with [†] to this award. The timeline will not allow AVI to wait for full manufacturing scale [†] cGMP drug product material, however the drug product used will be comparable and the assay method validated. The study and discussions with the FDA will be based on the IND already opened for drug product. Dosing will start at the [†]. Based on the pharmacokinetics, safety and general tolerability, [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] clinical study report; study conducted with research scale cGMP drug product.

3.3.2.1 Clinical Site and Local Laboratory Activities: The study will be planned and executed at an audited, selected [†] Clinical Research Facility with support from a fully CLIA accredited laboratory. From initiation onward the site(s) will be monitored through to study completion and site close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

Final report describing [†] clinical study conducted with research scale cGMP drug product manufactured at a cGMP-compliant facility.

3.3.2.1.1 Contracts and Budget: Contract and budget will be negotiated and agreed with the [†] CRO and supporting laboratories.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All contracts (site and laboratories) to permit study to be executed are agreed and signed.

3.3.2.1.2 Final Protocol to FDA; [†] submissions: Final [†] protocol submitted to FDA, [†]; feedback received and incorporated prior to study initiation.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All approvals received before initiation of clinical study.

3.3.2.1.3 Site Activities: First Subject In to Last Subject Out: The study will be planned and executed at an audited, selected [†] Clinical Research Facility. Site will be involved with review of study specific documentation and trained prior to first subject first visit. All interactions with site will be documented. Regular site monitoring will be planned and documented to ensure data has been verified and entered in a timely fashion, while ensuring subject safety. Any compliance issues will be raised to the clinical team for response.

Period of Work: Approximately [†] (e.g. [†]).

Deliverable: [†] clinical study conducted under cGCP and completed on schedule, within budget.

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3.3.2.1.4 Site Close Out: After completion of the last subject last visit, all data queries will be completed by the site and/or laboratory, previously validated database locked, analyses run, and draft study report prepared. In parallel formal close out of the clinical site, with disposal of unused drug supplies and completion of all outstanding documentation will occur.

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: All open queries and action items associated with clinical study execution are completed and documented in a site close out visit report.

3.3.2.2 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirming that subcontractors are trained to the study and ready to perform services.

3.3.2.2.1 [†] Method Validation: Feasibility studies have proven a [†] method acceptable for the determination of drug levels in [†] matrices. Each component of the study drug is assayed independently. The method will be validated (GLP) in matrices corresponding to samples specified by the clinical study protocol for pharmacokinetic analysis [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validated [†] assay for drug levels in [†] matrices.

3.3.2.2.2 Clinical Research Organization and Data Management: The CRO is key to study success. Their team along with AVI personnel is responsible for site start up activities, site training, and study execution, including data collection and management. The statistical support is part of the CRO. This group and Data Management will develop the plans necessary for data collection, query management, data analysis and quality checks. They will prepare reports for the [†] reviews. The final clinical study report will be written by CRO personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Executed contract between AVI and CRO.

3.3.2.2.3 Central Laboratory Services and Data Transfer: Exploratory [†] accessioning and analyses will each be conducted at a central lab facility. Data from each will be sent to data management vendor for inclusion in final study report.

Period of Work: Approximately [†] (e.g. [†]).

Deliverable: Laboratory data report.

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3.3.2.2.4 [†]: An independent [†] will be appointed to oversee and confirm dose escalation decisions. A [†] charter will be prepared and agreed with [†] members, a contract developed and a kickoff meeting and then dose escalation meetings with open and closed sessions. Members of the [†] will be available to review safety data and confirm or reject dose escalation to the next higher dose.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Decision to dose escalate continue or stop study as documented in meeting minutes.

3.3.2.2.5 Provide Electronic Data Management with Access to US Government: Enable [†] web portal with secure access to assigned study, company, vendor and USG personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Functional secure EDC portal access.

3.3.2.2.6 Drug Warehousing and Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.3.2.3 Study Documents for Clinical Sites and Final Study Report: The Clinical Research Organization (CRO) is responsible for preparing and providing to AVI for review all appropriate study specific documents, except the clinical protocol. Upon AVI authorization the CRO will send these documents to the sites in preparation for study start. Additionally, should any unexpected or serious safety events be reported, the CRO will document, discuss with AVI medical monitor, and complete the appropriate forms. At the study end, the CRO will prepare the tables, listings and figures and draft the final study report which will then be finalized with AVI input.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.3.2.3.1 Prepare and Distribute Study Documents: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], safety reporting, and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All study related documents including but not limited to: study plan and timeline, eCRF completion guidelines, monitoring reports, protocol compliance tracking, communication plan, meeting minutes, training materials and logs, drug accountability logs and final study report.

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3.3.2.3.2 Final Study Report: Prepare compliant and complete final clinical study report

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Submission ready final clinical study report.

3.3.2.4 Regulatory Submissions and Templates: The near final draft clinical protocol, FDA Form 1571, FDA Form 3674, FDA Form 1572, information on the investigators (including a copy of the CV of the Principal Investigator), study facility, and [†] will be submitted as an [†] for review by the FDA. An electronic template that is compliant with electronic submission requirements will be used for the protocol. Other "Essential Documents" specified by the ICH guideline on Good Clinical Practice and 21 CFR will be collected and reviewed for compliance. The clinical study will be registered on www.Clinicaltrials.gov or an equivalent public access database.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA Letter confirming that it is "Safe to Proceed" with the clinical study.

3.3.2.5 GCP Audits: Clinical data and document quality checks are carried out by clinical monitors during routine monitoring of each clinical study, as required under GCP. See section 3.2.1.3 for general description of quality Audits and Review. Quality Audits performed by experienced auditors from the QA Unit at clinical investigational sites (hospitals, etc.) are Direct Impact audits that will be specifically designed to verify compliance with GCP requirements and local and international regulatory regulations and guidelines. Audits will include contractor site selection audit, study audits during the study and an end of study audit. Audit documentation will be managed and archived in the EDMS

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit report are completed and satisfactory responses to audit findings are received from CRO's clinical facilities and [†] laboratories testing drug product in clinical studies. GCP-compliant clinical studies will occur using QA-approved protocols that meet regulatory and Institutional Review Board, HIPAA and USG requirements. Validated [†] methods are used for testing clinical samples.

3.3.2.6 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.3.3 Store Drug Product from Clinical Lot for 2 Years Past End of Study: Samples from the drug product batches used in the [†] clinical study will be stored under specified controlled storage conditions for 2 years past the completion of the study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Store samples of drug product used in [†] clinical study.

3.3.3.1 Initiate Drug Product Storage at Drug Distributor Warehouse: Drug product from the clinical trial will be retained for at least 2 years past the end of the clinical study end. These samples will be held at the recommended storage temperature in a secured refrigerated unit that is calibrated and monitored.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Store samples of drug product used in [†] clinical study

3.3.3.2 cGMP Audits: See section 3.2.3.1.3 Quality Audits and Review for general description of quality audits and section 3.2.4.1.4 for description of cGMP audits. Audits occur, audit reports are completed and satisfactory responses to audit findings are received from the subcontract facility storing and distributing AVI-6002 drug product for subsequent clinical use. Release and shipping of clinical supplies to clinical facilities will occur using QA-approved procedures that are compliant with GCP and local and international regulatory requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit report are completed and satisfactory responses to audit findings are received from the CMO drug product storage facility and conditions are acceptable for drug product lots for subsequent distribution for clinical use.

3.3.3.3 Project Management, Operations and Oversight: Oversight of warehouse storage of drug product will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.4. Stability Studies: Samples from the [†] (drug substance and drug product) and [†] scale (drug substance), will be placed on a stability study at recommended storage temperature and an elevated temperature as per ICH guidelines for a minimum of [†] consistent with the RFP. A final stability report will be written by the Contract organization that performs the stability studies.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Samples of drug substance and drug product set up for [†] stability studies.

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3.3.4.1 Contract Analytical Lab, Method Transfer, Short Term Stability of Drug Product at Dilutions for Clinical Study: Identify infusion sets, short term stability for at least [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Report on short term stability of drug product under conditions of clinical study.

3.3.4.2 Contract and Initiate [†]: These studies will confirm the stability of the regular [†]. These studies are expected to confirm result from previous stability studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Ongoing stability studies of [†].

3.3.4.3 Refine Stability Indicating Analytical Methods for Drug Substance and Drug Product: Forced degradation studies will identify degradants using HPLC/mass spectrometry. Once peak retention times are matched to degradant/impurity ID, stability program will utilize validated HPLC methods.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of analytical method development for Drug Substance and Drug Product.

3.3.4.4 24 Months Stability Studies Drug Product: Drug substance and the resultant drug product will be placed on a stability study at recommended storage temperature and an elevated temperature as per ICH guidelines for a minimum of [†] consistent with the RFP. This is applicable to cGMP materials made at both the [†] scales. A final stability report will be written by the Contract organization that performs the stability studies.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Ongoing [†] study with drug product prepared for [†] clinical study in CLIN0001.

3.3.4.5 Ongoing Quality Audits and Review including [†] Stability Programs: Drug substance and the resultant drug product will be placed on a stability study at recommended storage temperature and an elevated temperature as per ICH guidelines for a minimum of [†] consistent with the RFP. This is applicable to cGMP materials made at both the [†] scales. A final stability report will be written by the Contract organization that performs the stability studies See section 3.2.3.1.3 Quality Audits and Review for a general description of quality audits and section 3.2.4.1.4 for a description of cGMP audits. cGMP audits occur, reports are completed and satisfactory responses to audit findings are received from subcontract laboratories conducting stability studies. Analytical testing occurs using QA-approved validated analytical methods and stability specifications compliant with compendia and other regulatory requirements.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Audit report completed and satisfactory responses to audit findings received. Stability data are reported at regular intervals and reviewed by AVI.

3.3.4.6 Ongoing Program Management, Operations and Oversight including [†] Stability Programs:

Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress As part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a [†] basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.5 End of [†] FDA Meeting: AVI will request an End of [†] Meeting to discuss the future development plan including design of the [†] and the application of the [†] as soon as the data from the first clinical study is available, and appropriate questions of the agency can be formulated to enable the further clinical development. Agreement will be sought on fixed dose combination drug products, toxicology, toxicokinetics, clinical and pharmaceutical development of the drug substance and drug product, [†] development and review, with advanced notification of USG Program Office. The scheduling will depend on FDA, but the meeting should occur within 75 days of the formal request, and the briefing book will be sent to the FDA, at least 4 weeks ahead of the meeting. FDA feedback will be incorporated into the subsequent development plans. AVI's regulatory affairs staff will plan, prepare and compile the submission documents using electronic templates and e-publishing techniques; documents will be managed and stored electronically using the EDMS.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI submits an End of [†] Meeting Request Letter and Briefing Document to the FDA, participates in the meeting with FDA and prepares meeting notes. AVI reviews the FDA's official Meeting Minutes to assure that key elements of the discussions and agreements reached are documented. The FDA's requirements and expectations for the appropriate regulatory procedural enhancements leading to a potential [†] are clear.

3.3.5.1 [†] FDA Meeting Request [†], Preparation of Briefing Documents: Just before the completion of [†], AVI's regulatory affairs staff will manage, prepare and compile the [†] Meeting Request Letter and Briefing Document, with key components being provided by the research and development staff and subcontractors. The submission will be prepared using electronic templates, published using e-publishing techniques and all documents will be managed and controlled in the EDMS. The [†] Meeting will be planned and held, then AVI will prepare Meeting Notes that will be submitted to the FDA. The FDA's official Meeting Minutes will be reviewed for clarity and agreement with AVI's understanding of the outcomes. As necessary, AVI will continue proactive dialogue with the FDA by mutually convenient means.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] Meeting Request Letter and Briefing Document submitted to the FDA. A meeting date is agreed and the meeting (with participation of appropriate USG representatives) is planned.

3.3.5.2 FDA Meeting, Minutes, Follow up: AVI and USG representatives will attend the End of [†] Meeting. Agreement will be sought on a variety of development and regulatory procedural topics including for example applicability of fixed dose combination drug product requirements, toxicology, toxicokinetics, clinical and pharmaceutical development of the drug substance and drug product, [†] development and review FDA feedback will be incorporated into the subsequent development plans.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The [†] Meeting with the FDA occurs. AVI's Meeting Notes and the FDA's Meeting Minutes are prepared and reflect mutual agreements and understandings of the requirements for further development and the applicable regulatory procedures.

3.3.5.3 [†] FDA Meeting (CMC-focused): AVI will request a [†] Meeting to discuss the future development plan, specifically the approach for [†]. Agreement will be sought on [†], with advanced notification of USG Program Office. The scheduling will depend on FDA, but the meeting should occur within [†] of the formal request, and the briefing book will be sent to the FDA, at least [†] ahead of the meeting. FDA feedback will be incorporated into the subsequent development plans. AVI's regulatory affairs staff will plan, prepare and compile the submission documents using electronic templates and e-publishing techniques; documents will be managed and stored electronically using the EDMS.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: AVI submits a [†] Meeting Request Letter and Briefing Document to the FDA, participates in the meeting with FDA and prepares meeting notes. AVI reviews the FDA's official Meeting Minutes to assure that key elements of the discussions and agreements reached are documented. The FDA's requirements and expectations for the appropriate approach to [†], leading to a potential [†] are clear.

3.3.6 Complete [†] Clinical Trial and [†]: AVI will complete a [†] study to assess safety, tolerability and pharmacokinetics in [†] (RFP 3.3.2). The results from this first clinical study will be submitted to FDA as a supplement to the IND as soon as the data is available and the appropriate study reports are prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct and complete [†] clinical trial Submission of an [†] containing the Final Study Report of the [†] Clinical Trial and other [†] as needed to support continuing nonclinical, pharmaceutical and clinical research and development.

3.3.6.1 Prepare for and Meet with FDA to Discuss [†]: Due to the complexity and uncertainty about the FDA's expectations and requirements for [†] approval using the [†], AVI's regulatory affairs group

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will plan, request and manage a specific, [†] Meeting with the FDA and other interested USG agencies to discuss the application of the [†]. A Meeting Request Letter and Briefing Document will be prepared and submitted at least 4 weeks ahead of the meeting. AVI will prepare Meeting Notes and will review the FDA's official Meeting Minutes to assure agreement on the issues discussed. If necessary, further clarifications may be requested in writing. AVI will continue an open dialogue with the FDA and USG agencies involved and document those discussions.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Meeting Request and Briefing Document, attendance at the [†] Meeting, AVI's Meeting Notes and FDA's official Meeting Minutes. Agreement with the FDA and USG agencies regarding the applicability and requirements for developing oligomeric drug products under the [†], and for [†] approval.

3.3.6.2 Prepare and Submit [†] and [†]: AVI will submit [†] containing appropriate research and development data to the FDA and provide notifications to USG Program Office The agreement of the FDA will be sought to submit the protocols for the [†] studies as well as the [†] safety study for [†] and the relevant protocols will be submitted. AVI's regulatory affairs staff will plan, prepare and manage all submissions as electronic documents using electronic templates, e-publishing techniques and the EDMS.

Periods of Work: Approximately [†] days (e.g. [†]) and approximately [†] days (e.g. [†])

Deliverable: [†] will be submitted as [†] and the FDA's review comments will be incorporated before finalizing study protocols. [†] will be submitted as research and development data reports are available in order to keep the IND as current as possible. Copies of major submissions and correspondence will be forwarded to USG, as required.

3.3.6.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.7 Deliver [†] of Clinical Material to US Government: A sample of the drug product used in the [†] clinical study will be provided to the USG.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample drug product used in [†] clinical safety study to USG.

3.3.7.1 Ship [†] to US Government: At the end of CLIN0001 at least [†] of the drug product(s) will be delivered to the recipient specified by the USG.

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Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] clinical safety study to USG.

3.3.7.2 Project Management, Operations and Oversight: Oversight of inventory and distribution will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

CLIN0001 Final Contract Modification: Move several W9113M-10-C-0056 contract tasks originally scheduled to occur in CLIN0002 into the schedule of CLIN0001 activities to provide TMT management with nonclinical and clinical data sufficient in scope and content to justify moving to a "Milestone B" TRL-7 acquisition status and a total product commitment effort.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient nonclinical and clinical data to justify moving to a "Milestone B" TRL-7 acquisition status and a total product commitment effort.

3.3.8. Refine [†]: The critical goal of these studies is to obtain concurrence with FDA on the [†] study to be conducted under the [†]. Critical viral parameters will be addressed in PK/PD studies of [†], and in monitoring [†], both conducted at USAMRIID. The correlation of the [†] from natural infections, will guide the format and goals of the [†] study. The [†] study will be discussed and refined with the FDA. AVI will submit the protocols for the [†] prior to subcontracting the studies to USAMRIID (the proposed vendor to be pre-qualified as acceptable for GLP-compliant studies). The final protocols and final study reports will be submitted to FDA as [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Establish model for [†] Studies with FDA.

3.3.8.1 Viral Time Course: Alternative Dosing Study: This study is designed to investigate the outcome of altering the drug dosing regimen on survival during an active infection. The current regimen is a single dose per day, the regimen being tested is [†]. In a [†] period the amount of circulating drug reduces over time to form a "trough" during which time there is less protection. By administering the dose in [†] the trough will be filled, possibly resulting in greater efficacy even at lower doses. It is also possible that by [†] the resultant reduction in Cmax will reduce potential [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report optimizing the dose regimen and detailing the viral timecourse of Ebola infection in [†].

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3.3.8.2 [†]: This study has multiple objectives, all of which will help determine how to scale for an appropriate dose in humans. The objectives are as follows: 1) To determine influence of viral infection on the [†] of AVI-6002 to determine potential [†] in infected humans. 2) To determine the relationship between tissue drug levels and virus load. 3) Single dose [†] studies in [†] to inform scaling of dose in future [†] study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report containing [†].

3.3.8.3 Delayed Time to Treatment in [†]: To determine the effect of delaying treatment initiation on viremia and survival in [†] infected with Ebola Zaire virus. This study is being moved forward to better address the customer's request for a drug that can be administered [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report containing the survival of [†] in the delayed time to treatment efficacy study.

3.3.8.4 Viral Time Course in [†]: This study is designed to satisfy multiple questions regarding the effect of varying drug dosing regimens and viral and drug distribution during an active infection. The split objectives are as follows: 1) To better understand the [†] of EBOV infection. Studies are designed to evaluate [†] as a function of time post infection. To understand the relationship between distribution and concentration of AVI-6002 in sites of viral replication in a non-adapted EBOV infected [†]. Studies are designed to compare viral load in [†] following lethal challenge with EBOV. 2) To improve the dose regimen studies include [†] at [†] compared to [†] dosing of [†] and [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report optimizing the dose regimen and detailing the viral timecourse of Ebola infection in [†].

3.3.8.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.3.9 Phase 2 Multidose Dose Escalation Clinical Study: A [†] Volunteers. A goal for this study is to establish a [†], the intended therapeutic schedule. [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete Phase 2 clinical study and issue final clinical study report.

3.3.9.1 Protocol [†] Approval: Full [†] in parallel; AVI will answer any questions and amend protocol if necessary. The Amended protocol will be submitted to the [†] for approval prior to and notification of site(s) start study. All required information about the investigator, site, testing laboratories and CRO responsibilities will be submitted to the FDA prior to study start at any site.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA, Ethics Committee and [†] approvals received before study start.

3.3.9.2 Clinical Site and Local Laboratory Activities: The study will be planned and executed at audited, selected [†] Clinical Research site(s) with support from selected, fully [†] accredited laboratory. Site and laboratory will have had satisfactory GCP/GLP audits and then site will be initiated, monitored through to study completion and close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

3.3.9.3 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and reports needed will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirm that subcontractors are trained to the study and ready to perform services.

3.3.9.4 Provide Documents to Clinical Sites and Complete Study Reports: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

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3.3.9.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.10 Conduct Nonclinical Studies: Nonclinical [†] completed to-date in CLIN0001 include [†].[†] studies and both the [†] studies are in progress. All of the above mentioned studies were originally included in the planned studies for CLIN0001 and all are completed or on schedule according to the baseline scheduled represented in the IMS.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited Final Reports provided from CROs.

3.3.10.1 Protein Binding: Determine the interactions and binding characteristics of the individual components of AVI-6002 with plasma proteins for [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited Final Report provided from CRO.

3.3.10.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.11 Drug Manufacturing, Warehousing & Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.3.11.1 Drug Warehousing & Distribution – [†]: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] days (e.g. [†])

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Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.3.11.2 GLP Manufacturing – Refine Animal Models: Manufacture of GLP material for the animal studies.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide GLP material on time to site(s) and keep adequate records.

3.3.11.3 GMP Manufacturing at CMO – [†]: Manufacture of GMP material for the [†] clinical studies.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide GMP material on time to site(s) and keep adequate records.

3.3.11.4: GMP manufacturing of drug product at CMO – fill finish. Manufacturing of each agent is performed at CMO qualified to perform fill finish of these materials.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide vialed material. Ship to drug distribution and warehouse site. Provide C of A.

3.3.11.5 Perform [†] for Drug Product for [†] and [†]. AVI will contract with a CRO to develop a [†] of the drug product that will [†]. Drug substance will need to be supplied and dependent upon the quantity needed this will either be manufactured in-house or at a CMO. This development will occur on [†] in its entirety and knowledge learned from that development will be applied to the other [†] Previous experience in [†].

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Development Reports.

3.3.11.6 **Transfer Analytical Methods:** The [†] for quantifying API concentration and stability assessment will be transferred to the CRO. This will include supporting the CRO with reference solutions and materials to enable them to provide product assessment during the development

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Tech transfer report.

3.3.11.7 Product characterization and [†]: Drug substance product characteristics will be determined including differential [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†], report.

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3.3.11.8 Optimization of [†] Cycle: From the preliminary formulation studies the two best candidates will undergo [†] and these studies will be thoroughly evaluated for [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†], report.

3.3.11.9 Accelerated Stability Studies Leading to Selection of [†] Drug Product Formulation: [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†] formulation.

3.3.11.10 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.12 Quality Audits: The AVI Quality Management System provides for the quality oversight of the GMP, GLP and GCP work associated with this program. Subcontractors performing regulated work are audited as part of AVI's vendor qualification process. Quality audits are managed by the Director of QA and scheduled in accordance with the Audit Master Schedule. Auditors schedule travel to and from audits, write audit reports, provide lists of findings and make recommendations. Audit findings, recommendations and responses are reviewed by the Director of QA, the VP of Regulatory Affairs and QA, and the appropriate functional area management. Non-compliance issues are brought to the attention of the Chief Executive Officer (CEO). In addition, a QA Unit and Compliance Report is written monthly by the Director of QA. Audits will be conducted by experienced auditors from the Quality Unit. Audits employ a checklist approach, based on regulatory requirements and ICH guidelines; the checklists are customized to address the quality and regulatory requirements for each subcontractor facility and type of testing. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of subcontractors is also evaluated.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings.

3.3.12.1 Quality Audits – Facility for Animal Model Studies: Quality Audits of specialized Testing Facilities are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of on-site Direct Impact audits of the Testing Facility associated with performance of animal model studies in the BSL-4 laboratory. These are annual facility audits for the purpose of evaluating status and efforts towards GLP compliance, and for assuring that the level of compliance is appropriate to the work being performed. This task also includes annual facility audits of the CRO responsible for [†]. Audit Reports are prepared and circulated for internal review, then sent to the Testing Facility for review and response to any audit findings. Audits are closed out upon satisfactory resolution of any issues. Audit Certificates are prepared.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings

3.3.12.2 Quality Audits – Facility for Nonclinical Studies: Quality Audits of Contract Research Organizations are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of an on-site Direct Impact facility audit of the CRO associated with performance of the planned nonclinical protein binding studies. An Audit Report is prepared and circulated for internal review, then send to the CRO for review and response to any audit findings. The audit is closed out upon satisfactory resolution of any issues. An Audit Certificate is prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings.

3.3.12.3 GCP Audits – [†]: Quality Audits of Contract Research Organizations are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of an on-site Direct Impact audit of the CRO associated with management of the [†]. It may be a qualification audit of a new CRO or a re-audit of a previously qualified CRO. An Audit Report is prepared and circulated for internal review, then send to the CRO for review and response to any audit findings. The audit is closed out upon satisfactory resolution of any issues. An Audit Certificate is prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CRO.

3.3.12.4 GMP Audits – CMOs: Quality Audits of Contract Manufacturing Organizations are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of Direct Impact qualification audits or re-audits of contract manufacturers of [†]. Note that a Quality Audit will be conducted of a CMO's first [†] run. It will include observation of the manufacturing process per cGMP/Q7 guidelines and will be documented with a report that will be added to the initial CMO audit report. Additional GMP audits include audits of those contract organizations associated with analytical method development and validations, and lot release and stability testing. It also includes audits of CMO associated with [†]. The audits may be a facility or process audit, performed on-site or by questionnaire, as appropriate. Audit Reports are prepared and circulated for internal review, then sent to the CMO for review and response to any audit findings. Audits are closed out upon satisfactory resolution of any issues. Audit Certificates are prepared.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMO.

3.3.13 Quality Document Review: Quality Assurance review of documents (such as protocols and study reports).

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol or batch record) or for finalization of deliverables for other functional areas (e.g. study reports). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing.

3.3.13.1 Document Review – Animal Model Studies: Quality Assurance review of documents (such as protocols and study reports) associated with animal model studies and [†] testing. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol) or for finalization of deliverables (e.g. study reports).

3.3.13.2 Document Review – Nonclinical Studies: Quality Assurance review of documents (such as protocols and study reports) associated with nonclinical protein binding studies. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol) or for finalization of deliverables (e.g. study reports).

3.3.13.3 Document Review – [†]: Quality Assurance review of documents (protocol, GCP audit schedule, study report, etc.) associated with the [†] Clinical Study. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol, investigator brochure) or for finalization of deliverables (e.g. study reports).

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3.3.13.4 Document Review – CMOs: Quality Assurance review of documents associated with manufacturing operations, performed at contract organizations, or in-house. This task also includes review of documents associated with characterization of material for use in animal model studies and nonclinical studies, as well as documents associated with validations, material specifications, lot release testing, and stability testing of lots for clinical use. It includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol or batch record) or for finalization of deliverables (e.g. study reports, lot records, release testing). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing. Certificates of Analysis.

3.3.13.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.14. Regulatory Submissions: [†] Clinical Information and Nonclinical Information Amendments will be submitted as soon as study reports are available to keep the [†] up to date.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] Information Amendments submitted to the FDA.

3.3.14.1 Protocols to FDA for Approval – Refine Animal Model: Protocol submitted to the FDA as an [†] amendment.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA approved protocol before initial dose of investigational material is administered.

3.3.14.2 Protocols to FDA for Approval – [†]: Protocol submitted to the FDA as an [†] amendment.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA approved protocol before initial dose of investigational material is administered.

3.3.14.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track compliance, report progress. Project progress and any issues relative to the development plan will be documented and addressed with the Product Development Team on at least a monthly basis.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Develop timeline, manage vendors, anticipate and resolve problems, track compliance, report progress. Project progress and any issues relative to the development plan will be documented and addressed with the Product Development Team on at least a monthly basis.

3.3.15 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall program are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.3.15.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3.3.15.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.3.15.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

3.3.16.1 Subunit Process Development and Qualification: The GMP production of [†] will be examined with a focus on improving the repeatability of the plant scale production process.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The development report will be delivered to the CMC archive and any resulting process improvements will be implemented at the CMOs.

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3.3.16.1.1 Development of [†] GMP Production Process: The GMP production of [†] will be examined with a focus on improving the repeatability of the plant scale production process.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The development report will be delivered to the CMC archive and any resulting process improvements will be implemented at the CMOs.

3.3.16.1.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring timely delivery of development reports.

3.3.16.2 Manufacture [†] to Support Additional Production: Oversees the production of the additional [†] required for the drug manufacture to support the new studies. It also encompasses the required storage and retest tasks.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] will be provided to Manufacturing to support the planned drug production.

3.3.16.2.1 Manufacture [†] to Support Additional Production: Oversees the production of the additional [†] required for the drug manufacture to support the new studies. It also encompasses the required storage and retest tasks.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] will be provided to Manufacturing to support the planned drug production.

3.3.16.2.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring timely delivery of subunits to support the planned drug production.

3.3.16.3 Continue [†]: The continued stability on [†] has been moved from CLIN0002 to CLIN001.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] report will be delivered to the CMC archive.

3.3.16.3.1 Continue [†]: The continued stability on [†] has been moved from CLIN0002 to CLIN001.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] report will be delivered to the CMC archive.

3.3.16.3.2 Non Labor Costs Continue [†]: Subcontractor costs associated with [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: N/A

3.3.17.1 Qualification of Analytical Methods: Validation of analytical methods suitable for [†] clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validation report

3.3.17.1.1 Qualification of Analytical Methods for Release of AVI-7539: Validation of analytical methods suitable for [†] clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validation report

3.3.17.1.2 Qualification of Analytical Methods for Release of AVI-7537: Validation of analytical methods suitable for [†] clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validation report

3.3.17.2 QC Analysis: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Release Testing results.

3.3.17.2.1 QC analysis of [†] AVI-7537 for [†]: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.2 QC analysis of [†] AVI-7537: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.3 QC analysis of [†] AVI-7539 for [†]: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.4 QC analysis of [†] AVI-7539: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.5 QC Support for [†] GMP: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.3 Stability Testing on [†] lots: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Stability Testing results.

3.4 CLIN0002: AVI will deliver the developmental therapeutic end item that has achieved [†] clinical trials, based upon CLIN0001, additional prior studies and all the associated regulatory requirements sufficient and in place to support this. This will comprise all those activities necessary for our candidate product to complete the USG Statement of Objectives in CLIN0002.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug product on which [†] clinical trials have been completed.

3.4.1: Prepare Drug Product for [†] clinical study and [†]. cGMP drug product for the [†] clinical trial and [†] will be manufactured from cGMP drug substance prepared at [†] scale in CLIN0001.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Vialed, released drug product for [†] clinical study and [†]. Audit reports.

3.4.1.1: Prepare Drug Product for [†] clinical study and [†]. cGMP drug product for the [†] clinical trial and [†] will be manufactured from cGMP drug substance prepared at [†] scale in CLIN0001.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Vialed, released drug product for [†] clinical study and [†].

3.4.1.2 Quality Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated with drug product manufacture. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMO. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch record), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing. Certificates of Analysis.

3.4.1.3: Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.4.2 Develop and Validate Analytical Assays for Drug Product: AVI will complete analytical methods development and validation for drug product and finalization of specifications for lot release of drug product. The development and validation of formulated product analytical test methods utilize the analytical test methods developed and validated for therapeutic drug substance, where applicable. The addition of compendial tests and limits for sterility, to those for appearance, identification, assay and impurities will meet the regulatory requirements for lot release and for the product lots in ICH-compliant stability testing programs. The Director of QA will participate in the review and approval of analytical test methods, analytical validation protocols and reports, and drug product specifications that comply with compendia and other regulatory requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete development of analytical methods, validation and specifications for drug product.

3.4.2.1 Drug Product Analytical Method Development and Validation: Drug product analytical development will exploit similarities between the drug substance and the drug product to accelerate development and minimize validation time. As with drug substance, multiple HPLC methods are required for purity identification. Includes vendor qualification, facilities and API process audits of batch records by AVI QA Unit. AVI will complete analytical methods development and validation for drug product and finalization of specifications for lot release of drug product. The addition of methods for sterility, to those for appearance, identification, assay and impurities will meet the regulatory scrutiny required for cGMP release and ICH stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete development of analytical methods for drug product, and audited validation report.

3.4.2.2 Refine Drug Product Lot Release Specification: Based upon the results from the CLIN0001 manufacturing experience product specifications for each of the drug substances and the drug product will be developed. For the individual drug substances these will be similar to those developed in CLIN0001 since [†] studies will have been based upon these specifications that were used in the IND. Refinement of the specifications will be made based upon new assay development and analysis of lots used in the [†] studies and clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Finalize specifications for each drug substance and drug product.

3.4.2.3 Quality Audits: Perform facility audits of analytical testing laboratories, and review of all documentation associated with drug product analytical assay method development and validation. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMO. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. validation protocols) or for finalization of deliverables (e.g. analytical study report). Approval of validated analytical methods.

3.4.2.4 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.3 Scale-up Manufacturing, Qualification and Validation of cGMP Manufacturing Process: Manufacturing goals will include scale-up of the raw material supply [†], as well as that of drug substance. Further suppliers will be qualified. AVI will initiate the development of the full manufacturing scale of [†] modular manufacturing, and initiate validation of [†]. The manufacturing facilities will be audited for compliance with cGMP and other quality and regulatory requirements by experienced auditors. The Director of QA will participate in the review and approval of process validation protocols and reports.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug substance for [†] clinical trials will be prepared. Release drug substance lots for [†] clinical trials manufactured using a validated process at a cGMP-compliant facility. Lots meet the AVI-approved API specification and have been tested using validated analytical methods.

3.4.3.1 [†] Manufacturing Scale-Up: As part of the scale up process the [†] manufacturing supply chain needs to be established to produce [†] on the scale required to support the intended manufacturing scale-up. The current production capacity [†] multiple manufacturers will be utilized. However, even this effort will require expansion of [†] facilities for [†] of the activated [†]. [†] are needed to be made at the [†] to support scale up activities.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Assured supply for [†] and other raw materials.

3.4.3.1.1 Contract Additional [†] Manufacturing and [†] Sites: Negotiate and sign contracts with the additional [†] manufacturing and [†] CMOs.

Period of Work: Approximately [†] days (e.g. [†]). *Assumption: This will be complete prior to the start of CLIN0002.*

Deliverable: Selection and contract finalization of additional [†] CMOs.

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3.4.3.1.2 Manufacture of [†]: Complete tech transfer with all new CMOs. Scale-up the [†] production process and manufacture the required [†] to support the drug substance manufacture.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Timely supply of [†] to support drug substance manufacture.

3.4.3.1.3 [†] Storage and Retest: Continue maintenance of purified activated [†] in commercial cGMP storage facility. Perform analytical testing prior to use if retest date has been reached.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] ready for API manufacture when needed.

3.4.3.1.4 Quality Audits and Review: Perform facility audits of CMOs, analytical testing laboratories, and storage facilities, as well as review of all documentation associated with [†] manufacture, testing and storage. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records, testing plans), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing).

3.4.3.1.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project plan compliance, report progress. Progress and any issues will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMT will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.3.2 Manufacturing Scale-Up, Large Scale Manufacturing and Validation: The API production process will be scaled from the [†] to [†]. The drug substance process will undergo process validation in which [†] lots of drug substance are made. The scales for validation will include the [†] and the [†] scale. All validation lots will be placed on stability. Material from the validation lots will be used to manufacture drug product for the [†] clinical trial. The Director of QA participates in the review and approval of process validation protocols and reports.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited validation report for large scale manufacturing at a suitably qualified CMO.

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3.4.3.2.1 Finalize drug substance manufacturing process. Based on experience from the CLIN0001 [†] cGMP production run and incorporating FDA guidance from the [†] meeting, examine and finalize the critical parameters for the drug substance production process.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Refined and finalized parameters for production.

3.4.3.2.2 Drug Substance Manufacturing Scale Up to [†]: From the [†] scale, the process will be increased to a [†]. The purpose of using a smaller reaction size in a larger capacity reactor is to control costs during clinical development, but enable future scale increases in already qualified equipment. This allows minimization of costs during the program and later enables production of RFP threshold quantities for commercial production. This [†] run could consist of several cycles in the solid phase synthesis process, but not a complete production run, in order to verify applicability of the process parameters at this scale.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Demonstration of [†] scale manufacturing process.

3.4.3.2.3 Validation of cGMP Drug Substance Manufacturing Process: A process validation protocol will be written and executed under the guidance of the CMO with direct input from AVI, using guidance from the FDA from the EOP2 meeting. Results of this validation will be reviewed and, if acceptable, approved. The protocol will contain acceptance criteria in order to evaluate the success. The Director of QA participates in the review and approval of validation protocols, validation reports, and master batch records,

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited validation report for drug substance manufacturing process.

3.4.3.3 Quality Audits: Perform review of documentation associated with validation of the cGMP drug substance manufacturing process. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records, validation protocols), ongoing evaluation of processes, or for finalization of deliverables (e.g. validation reports).

3.4.3.4: Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.4 Refine and Select Drug Product Formulation: AVI will continue to develop a [†] of the drug product that will enhance the [†] based upon product characteristics learned in CLIN0001. Drug substance will need to be supplied and dependent upon the quantity needed this will either be manufactured in-house or at a CMO. Knowledge learned from prior development will be applied to the USG contracted drug products. Previous experience in [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Decision on final formulation for drug product formulation.

3.4.4.1 Transfer Analytical Methods: The [†] method for quantifying API concentration and stability assessment will be transferred to the CRO. This will include supporting the CRO with reference solutions and materials to enable them to provide product assessment during the development.

Period of Work: Approximately [†] elapsed days (e.g. [†]).

Deliverable: Tech transfer report.

3.4.4.2 Product characterization and [†]: Drug substance product characteristics will be determined including differential [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on [†], report.

3.4.4.3 Optimization of [†]: From the preliminary formulation studies the two best candidates will undergo [†] and these studies will be thoroughly evaluated for [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on [†], report.

3.4.4.4 Quality Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated with drug product formulation development and new formulation drug product manufacture. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing).

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3.4.4.5 Accelerated Stability Studies Leading to Selection of [†] Drug Product Formulation: Conduct stability studies at high temperature to drive final decision on [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†].

3.4.4.6 Determine Extractables and Leachables: Determine if any chemical components are extracted or leached from containers, closures, or materials used in administration of the drug.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†].

3.4.4.7 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.5 Manufacture cGMP Material at Scale for Clinical Studies and Consistency Lots: Preparation of cGMP drug product for [†] clinical safety. Three drug product batches will be validated and all will provide material for stability studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] scale cGMP drug product manufactured for [†].

3.4.5.1 Drug Product Engineering Run: Drug product configuration and process will be transferred to CMO. An engineering run is planned with the first drug substance of the drug substances manufactured in CLIN0002 for the purposes of testing all fill finish capabilities including [†], formulation testing, and product testing for adherence to product specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Process suitable for GMP drug manufacture of commercial material.

3.4.5.1.1 Drug Product Engineering Run: An engineering run is planned with the first drug substance of the combination product manufactured in CLIN0002 for the purposes of testing all fill finish capabilities including [†], formulation testing, and product testing for adherence to product specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Successful tech transfer and final process suitable for GMP drug manufacture.

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3.4.5.2 Manufacture, Release, Label 3 Consistency Lots of Drug Product: A process validation protocol will be written and executed under the guidance of the CMO with direct input from AVI, using guidance from the FDA from the [†] meeting. Material produced at scale will be filled for the clinical lots and for the consistency lots at a size commensurate with the production scale of the contract manufacturing organization.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Released, labeled drug product for clinical trials. Audited validation report for drug product manufacturing process.

3.4.5.3 cGMP Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated with at scale drug product manufacturing and consistency lots. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days ([†])

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing).

3.4.5.4 Project Management, Operations and Oversight: The program will be managed by AVI personnel and consist of initial technology transfer and reduction to practice lots prior to cGMP production. Hands on training may be provided initially but after establishment of the process and successful manufacturing the program will be managed through conference calls, sites visits, audits, data and document review including specifications and comparison of release data with those specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.6 Stability Studies: Continuing stability studies from CLIN0001 and start of [†] ICH stability studies. Drug substance and Drug product will be evaluated according to ICH stability requirements. The duration of the stability program is [†], and it will exceed the minimum requirement in the statement of objectives and Target Product Profile (TPP) threshold. The stability program includes full term aging studies at [†] will not be performed on the drug substance, but will be performed on the lyophilized drug product.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies of [†] and validated drug substance have been initiated. Stability studies set up for cGMP drug product material manufactured for [†] safety studies.

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3.4.6.1 Stability on Drug Substance ([†] Stability Program Starts): Follow ICH guideline Q1A to acquire data to justify retest date at defined storage condition.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of stability studies from CLIN0001 and initiation of studies on validated drug substance.

3.4.6.1.1 Ongoing Stability on Drug substance: This is the completion of the drug substance stability program started in CLIN0001.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug substance.

3.4.6.1.2 Stability Studies Drug Substance ([†] Stability Program Starts): Each drug substance manufactured will be placed on a [†] stability program in order to demonstrate the long term product characteristics of the material. All cGMP lots made in CLIN0002 will be placed on stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug product.

3.4.6.2 Stability on Drug Product ([†] Stability Program Starts): Follow ICH guideline Q1A to acquire data on validation lots to justify expiration date at defined storage condition. All CLIN0002 cGMP drug product lots will be placed on stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug product.

3.4.6.2.1 Drug Product Stability Studies: Drug product manufactured to supply the pivotal animal efficacy and QTc clinical studies will be placed on stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability data for drug product for pivotal animal efficacy and QTc clinical studies.

3.4.6.2.2 Stability Studies Drug Product ([†] Stability Program): New drug product stability studies will be set up for [†]. Multiple temperature storage conditions will be examined to provide the storage conditions for optimal use.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug product.

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3.4.6.3 cGMP Audit: Perform facility audits of contract manufacturing organizations, and review of all documentation associated drug product stability studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. stability protocols) or for finalization of deliverables (e.g. analytical study report). Audited final report on stability and shelf life of drug product.

3.4.6.4 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.7 Stability Testing to Define Operational Storage (Time Temperature Indicator): Each drug product is [†], which makes room temperature storage feasible and reduces cold chain requirements, exceeding minimum requirement in the statement of objectives and TPP threshold. The scope of the stability studies will establish the Time Temperature Indicator (TTI), since it includes full term accelerated conditions. Based upon the results, a TTI can be established to support the product shipments. As part of the operational storage and distribution criteria, product shipments will be monitored for excursions during shipment using temperature monitoring devices.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies set up for [†] scale cGMP product material to establish TTI.

3.4.7.1 Conduct Stability Studies under [†]: These studies will be conducted at [†] temperature than the recommended storage condition to determine additional time that the material may exposed to harsher conditions without risk.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies completed to establish TTI.

3.4.7.2 Conduct Shipping and Transport Stability Studies: These studies will show that the drug product is stable under the actual conditions of shipping.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies completed to establish TTI.

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3.4.7.3 Quality Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated drug product stability studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. stability protocols) or for finalization of deliverables (e.g. analytical study report).

3.4.7.4 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.8 Conduct Nonclinical Studies: In addition to the multiple studies completed to date and forming the basis for the open IND, the studies since then and prior to this award that will supplement that IND, AVI will also complete further [†] studies, for example [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct [†] scale cGMP product material.

3.4.8.1 [†]:[†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final Report on [†].

3.4.8.2 [†]: [†] to provide data necessary for registration.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient [†].

3.4.8.3 [†] Mass Balance: [Mass balance study required to show fate of drug in [†]; required data for registration.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report from CRO on mass balance in the [†].

3.4.8.4 [†] in vivo Metabolism: Provide data on metabolism of drug in [†] model. Required for registration and determination if any metabolites are present that need to be monitored in preclinical and clinical trials.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report from CRO on in vivo metabolism in the [†].

3.4.8.5 [†]: This study was moved to 3.3.10.1 as part of the contract modification.

3.4.8.6 [†] Dose Range Finding Study: To determine the effect of treatment on the [†] development, with determination of appropriate dose levels for the definitive [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on [†] study.

3.4.8.7 [†] Study: The definitive study to determine the effect of treatment on the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on [†] study.

3.4.8.8 Quality Audits: Perform facility audits of animal testing facilities and [†] laboratories, and review of documentation, associated with GLP toxicology studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. Quality Assurance review of documents (such as protocols and study reports).

3.4.8.9 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.9 [†] Efficacy Studies in [†]: The [†] studies will confirm therapeutic efficacy at specific dose levels and expected exposures that will be mimicked in [†]. Using the currently filed IND, clinical safety and any animal data obtained during CLIN0001, any additional preclinical data, and based on the protocol developed with FDA as to the studies necessary under the [†], AVI will conduct the [†] studies, necessary to show protection against an [†] challenge by injection.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct NHP [†] studies using [†] scale cGMP product material.

3.4.9.1 [†] Efficacy Studies in [†] #1: The [†] studies will confirm therapeutic efficacy at specific dose levels and expected exposures that will be mimicked in [†].

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct NHP [†] studies using [†] scale AVI-6002 cGMP product material

3.4.9.1.1 [†] Acquisition and Acclimation: Prior to [†] protocols are reviewed by [†]. Once protocols are approved, [†]. [†] are held in quarantine to ensure acclimation to the laboratory setting and receive a final health evaluation. Finally, randomization and cage arrangements are finalized.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient [†] acclimated and released for first pivotal study to begin.

3.4.9.1.2 Conduct Study, Laboratory Analyses, Viral Sequencing: This is the "in-life" phase of the study involving [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of the [†] portion of the first [†] study.

3.4.9.1.3 Data Analyses, Final Study Report: Compile observations and unblind data. Statistical analysis and preparation of a final study report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Presentation of final study report.

3.4.9.2 [†] Studies in [†]: The [†] studies will confirm therapeutic efficacy at specific dose levels and expected exposures that will be mimicked in [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct NHP [†] studies using [†] scale AVI-6002 cGMP product material

3.4.9.2.1 [†] Acquisition and Acclimation: Prior to [†] protocols are reviewed by [†]. Once protocols are approved, [†] acquisition can take place. [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient [†] acclimated and released for second pivotal study to begin.

3.4.9.2.2 Conduct Study, Laboratory Analyses, [†]: This is the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of the [†] portion of the [†] study.

3.4.9.2.3 Data Analyses, Final Study Report: Compile observations and unblind data. Statistical analysis and preparation of a final study report.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Presentation of final study report.

3.4.9.3 Data Management: Full data management and statistical analysis plans will be developed by a qualified Contract Research Organization, and shared with the FDA (and USG) before studies completed. The CRO will monitor source documents (to the extent possible in a BSL4 environment), collect data, ensure all data queries are clarified, lock database, analyze and then reveal treatment allocation.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct analyses of pivotal efficacy studies for study reports.

3.4.9.4 GLP Audits: Perform facility audits of [†] testing facilities and [†] laboratories, and review of documentation, associated with [†] studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. Quality Assurance review of documents (such as protocols and study reports).

3.4.9.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project plan compliance, report progress. Progress and any issues will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.10 Activities to Achieve Pivotal Efficacy Studies: AVI will prepare and submit [†]. The Final Protocols for the [†] studies will also be submitted after the FDA responses are received from the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] submitted to the FDA.

3.4.10.1 [†] (Clinical, Nonclinical): [†] will be submitted as soon as study reports are available to keep the [†]. The Final Protocols for the [†] studies will also be submitted as [†] after the FDA responses are received from the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] submitted to the FDA.

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3.4.10.2 [†] (Drug Substance, Drug Product): [†] will be submitted as soon as data are available on the lots of drug substance and drug product that will be used in the [†] Studies are available. Additional [†] will be submitted as reports and data are available to keep the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Prepare and submit [†].

3.4.10.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.11 Request and Conduct [†] Meeting with the FDA: AVI will request an [†] to provide a summary of results of the [†] clinical studies and to discuss the [†] clinical development plan. The topic of designation as a [†]. A Meeting Request Letter and Briefing Document will be submitted to the FDA. Advanced notification of the meeting, plus copies of all meeting-related documents will be provided to the USG Program Office in a timely manner. After the meeting AVI's regulatory affairs staff will prepare and submit notes of the meeting as an [†]. The FDA's official Meeting Minutes will be reviewed to ensure that they reflect the same meeting outcomes and agreements as those documented by AVI.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] Request and Briefing Document submitted to the FDA. Participate in [†] meeting with FDA. Prepare notes of the meeting and review the FDA's official Meeting Minutes to assure that both the FDA and AVI agree on the outcomes of the discussion and agreements.

3.4.11.1 Prepare Meeting Request and Briefing Document: The Meeting Request Letter and Briefing Document will be prepared as soon as is feasible and submitted to the FDA at least one month in advance of the requested meeting date. Advanced notification of the meeting, plus copies of all meeting-related documents will be provided to the USG Program Office in a timely manner.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] Meeting Request Letter and Briefing Document submitted to the FDA.

3.4.11.2 [†]:[†].

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Submit request for [†] to the FDA.

3.4.11.3 FDA Meeting, Minutes and Follow Up: AVI will attend the [†] with the FDA. AVI will submit notes of the meeting to the FDA and ensure that the company is in agreement with the outcomes and agreements recorded in the FDA's official Meeting Minutes. Clarifications will be requested, as necessary. AVI will continue an open dialogue with the FDA as development continues.

Period of Work: Approximately [†] week (e.g. [†]).

Deliverable: AVI will provide copies of the company's notes and the FDA's official Meeting Minutes to the USG Program office.

3.4.11.4 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track compliance, report progress. Project progress and any issues relative to the development plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.12 [†]:[†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] clinical safety study to USG

3.4.12.1 Ship [†] to US Government: At the end of CLIN0002 at least [†] of the drug product(s) will be delivered to the recipient specified by the US Government.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] clinical safety study to USG

3.4.12.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.13 Phase 2 Multidose Dose Escalation Clinical Study: This study was moved to 3.3.9 as part of the contract modification.

3.4.14 [†] Clinical Study: AVI will conduct a [†]. A specialized [†], is expected to support efficient enrollment and evaluation. Subject accrual and treatment is scheduled for less than [†] months. The results will be available for the planning of the expanded [†] trial.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct [†] clinical study using [†] scale cGMP drug product material and issue final clinical study report.

3.4.14.1 Clinical Site and Local Laboratory Activities: Clinical sites and laboratories will be audited for compliance with GCP, selected and then initiated, monitored through to study completion and close out. The study will be planned and executed at audited, selected [†] Clinical Research site(s) with support from a fully [†] accredited laboratory. From initiation forward the site(s) will be monitored through to study completion and site close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

3.4.14.1.1 Contracts and Budgets: Contracts will be negotiated with vendors for the execution of this study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Signed contracts in place with all vendors before initiation of [†] clinical study.

3.4.14.1.2 [†] Approval: Full protocol will be submitted to [†] in parallel; AVI with CRO will answer any questions and amend protocol if necessary to ensure final ethics approval, and notification of site(s) prior to study start.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All approvals received before initiation of clinical study.

3.4.14.1.3 Site Activities First Patient in to Last Patient Out: The study will be planned and executed at an audited, selected [†] Clinical Research Facility. Site will be involved with review of study specific documentation and trained prior to first subject first visit. All interactions with the site will be documented. Regular site monitoring will be planned and documented to AVI (or Contract Research Organization staff) will monitor conduct of the [†] study to ensure data has been verified and entered in a timely fashion, while ensuring subject safety. Any compliance issues will be raised to the clinical team for response.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete in life portion of [†] study and complete electronic case report forms on schedule and within budget.

3.4.14.1.4 Site(s) Close Out: After completion of the last subject last visit, all data queries will be completed by the site and/or laboratory, previously validated database locked, analyses run, and draft study report prepared. In parallel formal close out of the clinical site, with disposal of unused drug supplies and completion of all outstanding documentation will occur.

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Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: All open queries and action items associated with clinical study execution are completed and documented in a site close out visit report.

3.4.14.2 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and necessary reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirm that subcontractors are trained to the study and ready to perform services.

3.4.14.2.1 Clinical Research Organization and Data Management: The CRO is key to study success. Their team, along with AVI personnel, is responsible for site start up activities, site training, and study execution, including data collection and management. The statistical support is part of the CRO. This group and Data Management will develop the plans necessary for data collection, query management, data analysis and quality checks. They will prepare reports for the [†] reviews. The final clinical study report will be written by CRO personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Executed contract between AVI and CRO.

3.4.14.2.2 Central Laboratory Services and Data Transfer: [†] and analyses will each be conducted at a central lab run at one facility. Data from each will be sent to data management vendor for inclusion in final study report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Laboratory data reports provided to data management vendor.

3.4.14.2.3 [†]: An independent [†] will be appointed to oversee and confirm dose escalation decisions. A [†] charter will be prepared and agreed with [†] members, a contract developed and a kickoff meeting and then dose escalation meetings with open and closed session. Members of the [†] will be available to review safety data and confirm or reject escalation to the next higher dose.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Decisions to dose escalate, continue or stop study as documented in meeting minutes.

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3.4.14.2.4 Provide Electronic Data Management with Access to US Government: Enable [†] with secure access to assigned study, company, vendor and USG personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Functional secure [†] access.

3.4.14.2.5 Drug Warehousing and Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.4.14.3 Provide Documents to Clinical Sites and Complete Study Reports: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.4.14.3.1 Prepare and Distribute Study Documents: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All study related documents including but not limited to: study plan and timeline, [†] guidelines, monitoring reports, protocol compliance tracking, communication plan, meeting minutes, training materials and logs, drug accountability logs and final study report.

3.4.14.3.2 Final Study Report: Prepare Submission ready final clinical study report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The Final Study Report will be submitted to the FDA as an [†]. Submit compliant and complete final clinical study report.

3.4.14.4 GCP Audits: Perform Quality Audits of Contract Research Organization and review of documentation associated with management of the [†]. See section 3.8.1 Quality Audits and Review for a general description of quality audits. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CRO. Quality Assurance review of documents (such as the study protocol, investigator brochure, and clinical study report).

3.4.14.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.15 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall program are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable. In addition AVI will continue to implement enhancements to the Quality Systems Approach already in place, including installation of a secure 21 CFR Part 11 compliant EDMS and preparation for electronic submission of documents to the FDA. The EDMS will be utilized for document management and control, including collaborative authoring of study reports and eCTD text for the [†], revision and versioning control with metadata for audit trails, and secure document repository. The EDMS will provide authorized representatives of USG electronic access to program status information. The use of eCTD compliant document templates and completed reports for electronic submissions to the FDA will be managed, controlled, archived and regulated under the Quality System in the EDMS.

Period of Work: Concurrent with all CLIN0002 activities. Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.4.15.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0002 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3.4.15.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Concurrent with all CLIN0002 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.4.15.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0002 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

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3.4.15.4 EDMS and QA: AVI will continue to store all documents on the validated EDMS and preparation for electronic document submission to the FDA. AVI will train all pertinent staff on EDMS and Quality Assurance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.5 CLIN0003: AVI will deliver the developmental therapeutic end item that has achieved [†] Clinical Study, based upon CLIN0001 and CLIN0002 (recognizing that some activities will be concurrent), additional prior studies and all the associated regulatory requirements sufficient and in place to support this. This will comprise all those activities necessary for our candidate drug product to complete the USG Statement of Objectives in CLIN0003.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug product on which [†] Clinical Study has been completed.

3.5.1 Complete Pivotal Efficacy Studies: This has been moved to CLIN0002 3.4.9.1 and 3.4.9.2.

3.5.2 [†]: Continue to implement enhancements to the Quality Systems Approach already in place, including installation of a secure 21CFR Part 11 compliant EDMS and preparation for electronic submission of documents to the FDA.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Submit the quality amendment to FDA as a supplement to the AVI-6002 [†].

3.5.2.1 Write and Submit [†]: Update information stored on EDMS and preparation for electronic submission of documents to the FDA.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Submit the quality amendment to FDA as an [†].

3.5.2.2 Respond to FDA Questions: Develop and provide response to any questions or recommendations from FDA following filing of [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Submit to FDA as an [†].

3.5.2.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report project progress. As part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget

3.5.3 [†] Study: Using the currently filed AVI-6002 [†], clinical safety and any [†] data obtained during CLIN0001 and CLIN0002, AVI will initiate the [†] Study in [†] using the protocols agreed with FDA, while ensuring all necessary [†] study requirements such as [†] review and approval. AVI will conduct this [†]. FDA concurrence that this will be sufficient for the safety database to [†] will be sought.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct and audit [†] study and issue final study report.

3.5.3.1 Clinical Site and Local Laboratory Activities: The study will be planned and executed at audited, selected [†] Clinical Research site(s) with support from a fully [†] accredited laboratory. From initiation forward the site(s) will be monitored through to study completion and site close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

3.5.3.1.1 Contracts and Budgets: Contracts will be negotiated with vendors for the execution of this study.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Signed contracts in place with all vendors before initiation of [†] clinical study

3.5.3.1.2 [†] **Approval**: Full protocol will be submitted to [†] in parallel; AVI with the CRO will answer any questions and amend protocol if necessary to ensure final ethics approval and notification of site(s) prior to study start.

Period of Work: Approximately [†] months (e.g. [†])

Deliverable: FDA, Ethics Committee and [†] approvals received before initiation of the [†] safety study.

3.5.3.1.3 Site Activities First Patient in to Last Patient Out: The study will be planned and executed at an audited, selected clinical sites. Sites will be involved with review of study specific documentation and trained prior to first subject first visit. All interactions with the sites will be documented. Regular site monitoring will be planned and documented to AVI (or Contract Research Organization staff) will monitor conduct of the [†] study to ensure data have been verified and entered in a timely fashion, while ensuring subject safety. Any compliance issues will be raised to the clinical team for response.

Period of Work: Approximately [†] months (e.g. [†]).

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Deliverable: Complete in life portion of pivotal safety study and complete electronic case report forms on schedule and within budget.

3.5.3.1.4 Site(s) Close Out: After completion of the last subject last visit, all data queries will be completed by the site and/or laboratory, previously validated database locked, analyses run, and draft study report prepared. In parallel formal close out of the clinical site, with disposal of unused drug supplies and completion of all outstanding documentation will occur.

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: All open queries and action items associated with clinical study execution are completed and documented in a site close out visit report.

3.5.3.2 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and necessary reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirm that subcontractors are trained to the study and ready to perform services.

3.5.3.2.1 Clinical Research Organization and Data Management: The CRO is key to study success. Their team, along with AVI personnel, is responsible for site start up activities, site training, and study execution, including data collection and management. The statistical support is part of the CRO. This group and Data Management will develop the plans necessary for data collection, query management, data analysis and quality checks. They will prepare reports for the [†] reviews. The final clinical study report will be written by CRO personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Executed contract between AVI and CRO.

3.5.3.2.2 Central Laboratory Services and Data Transfer: [†] and analyses will each be conducted at a central lab facility. Data from each will be sent to data management vendor for inclusion in final study report.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Laboratory data reports provided to data management vendor.

3.5.3.2.3 [†]: An independent [†] will be appointed to oversee and confirm dose escalation decisions. A [†] will be prepared and agreed with [†] members, a contract developed and a kickoff meeting and then dose escalation meetings with open and closed session. Members of the [†] will be available to review safety data and confirm or reject escalation to the next higher dose.

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Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Provide safety oversight for pivotal safety study. Decisions to dose escalate, continue or stop study as documented in meeting minutes.

3.5.3.2.4 Provide Electronic Data Management with Access to US Government: Enable [†] with secure access to assigned study, company, vendor and USG personnel.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Functional, secure [†] access.

3.5.3.2.5 Drug Warehousing and Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.5.3.3 Provide Documents to Clinical Sites and Complete Study Reports: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.5.3.3.1 Prepare and Distribute Study Documents: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All study related documents including but not limited to: study plan and timeline, eCRF completion guidelines, monitoring reports, protocol compliance tracking, communication plan, meeting minutes, training materials and logs, drug accountability logs and final study report.

3.5.3.3.2 Final Study Report: Prepare submission ready final clinical study report.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Submit compliant and complete final clinical study report.

3.5.3.4 GCP Audits: Audits will be performed of Clinical Study Sites.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Audits will occur, audit reports completed and satisfactory responses to audit findings will be required from clinical sites. Study reports and data listings will be reviewed and approved by the CRO's QA unit and by AVI's monitor and QA Unit.

3.5.3.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.5.4 Refine and Select Formulation and Delivery System: AVI will continue the assessment of stability for the validation lots prepared in CLIN0002. The drug kit per treatment will comprise [†]. The storage of the kit will be at room temperature (15°C to 30°C). This drug product kit meets the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Finalize the drug kit components for drug product.

3.5.4.1 Determine Configuration for Market: All details of the commercial formulation are finalized ([†]).

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Finalize the drug kit components for AVI-6002 product.

3.5.4.2 Identify Manufacturer for Packaging Final Product: Establish contract for assembling final marketing packages.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Finalize the vendor for manufacture, labeling and packaging of AVI-6002 product.

3.5.4.3 Continue Drug Substance and Drug Product Stability Studies: Continue drug substance and drug product stability studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Continue stability for drug substance and drug product.

3.5.4.4 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.5.5 Deliver [†] to US Government: Deliver at least [†] of product, from the lot used for the [†] study.

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Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] study to USG.

3.5.5.1 Deliver [†] to US Government: At the end of CLIN0003 at least [†] of the drug product(s) will be delivered to the recipient specified by the USG.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] study to USG

3.5.5.2 Project Management, Operations and Oversight: Oversight of inventory and distribution will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.5.6 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall program are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.5.6.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0003 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3. 5.6.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Concurrent with all CLIN0002 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.5.6.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0003 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

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3.5.6.4 EDMS and QA: AVI will continue to store all documents on the validated EDMS and preparation for electronic document submission to the FDA. AVI will train all pertinent staff on EDMS and Quality Assurance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.6 CLIN0004: AVI will deliver the FDA approved therapeutic end item including all New Drug Application and Approval activities resulting in the delivery of at least [†], based upon CLIN0001, CLIN0002 and CLIN0003 (recognizing that some activities will be concurrent), additional prior studies and all the associated regulatory requirements sufficient and in place to support this. This will comprise all those activities necessary for [†] drug product to complete the USG Statement of Objectives in CLIN0004.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug product approved by FDA.

3.6.1 [†] Meeting with the FDA: A [†] Meeting with the FDA will be requested and a Briefing Document submitted approximately one month in advance of the meeting. The FDA will schedule the meeting within 60 days of the request. The purpose of the [†] Meeting is to reach agreement on the electronic format and content of the [†]. The [†] will also be discussed at this meeting. AVI will prepare notes of the meeting that will document the discussion and agreements with the FDA; the notes will be submitted to the FDA. The FDA will issue official Meeting Minutes. AVI will follow up to request clarifications, as needed.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI prepares and submits Request Letter and Briefing Document, participates in the [†] meeting with the FDA, prepares notes of the meeting that are submitted to the FDA.

3.6.1.1 Prepare Meeting Request and Briefing Documents: The [†] Meeting Request Letter and Briefing document will be prepared and submitted as soon as is feasible after the completion of dosing in the clinical trials approximately [†] ahead of the meeting. Advanced notification of the meeting, plus copies of all meeting-related documents will be provided to the USG in a timely manner.

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: AVI [†] Meeting Request Letter and Briefing Document are submitted to the FDA.

3.6.1.2 [†] Meeting, Minutes and Follow Up: AVI will participate in the [†] with FDA, take notes and obtain official minutes, following up on any action items due. AVI will provide copies of the FDA's Meeting Minutes to USG.

Period of Work: Approximately [†] weeks (e.g. [†]).

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Deliverable: AVI's [†] Meeting notes and the FDA's official Meeting Minutes.

3.6.1.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMT will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.2 Prepare, Submit and FDA Review of [†]: AVI will electronically submit an [†] that meets the USG's Target Product Profile. By using eligibility as a small business enterprise, and employing regulatory procedural relief benefits due [†], AVI is planning for the [†] to be prior to the completion of the contractual period proposed. During the FDA's review, AVI will remain ready to respond promptly to any questions that arise by using secure email correspondence. The USG will be kept fully informed of progress.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI prepares and electronically submits an [†] that meets the FDA's requirements for review and validation.

3.6.2.1 Complete and Submit [†] and Respond to FDA Review Comments: AVI will complete and submit an [†] to the FDA; and respond in a timely fashion to Information Requests and other comments from the FDA reviewers.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: An [†] that has been submitted electronically to the FDA and accepted for filing as an appropriately structured electronic submission. Responses to Requests for Information and the [†] from the FDA will be answered promptly.

3.6.2.2 Project Management and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.6.3 [†] and Response to FDA [†]: Given the issues faced by the FDA [†], it is likely that the FDA [†]. AVI will attend and participate in an ACM, and respond promptly to any questions in the [†] approval occurs.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Responses to Requests for Information from the FDA will be submitted promptly. AVI will prepare a Briefing Document and presentation materials for an [†]. Draft notes of the [†] will be prepared.

3.6.3.1 [†]: AVI will plan and prepare and, once confirmed, attend and participate at [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI will prepare a presentation and Briefing Document in advance of the ACM.

3.6.3.2 Prepare and Submit Complete Response to [†]: At the conclusion of their review, the FDA will issue a [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete Response will be made to any questions asked by the FDA.

3.6.3.3 Project Management and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.3.4 [†]: AVI will receive formal confirmation [†]. AVI will submit [†] and participate in the final negotiations of the [†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Receipt of the [†]. A copy will be sent to the USG Program office.

3.6.4 [†] in Compliance with FDA Requirements: The [†]. The [†], or in the electronic format required by the FDA at that time. The [†] will have been submitted to the FDA in the [†] at that time.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Prepare [†].

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3.6.4.1 Structured [†] Review and Responses: Preparation of the draft [†] (i.e. the physician's information and patient information leaflet) will be started before [†] to facilitate discussion with the FDA and information will continue to be added up [†]. Two versions are required to be submitted in the [†], one of which is annotated with the source data for each statement. Both versions are submitted electronically in the required XML format. During review by the FDA Division and by [†], AVI will respond to comments promptly. At the conclusion of the FDA review, AVI will resubmit the final version of the agreed labeling as an SPL (XML) format. [†] will be sent to the USG Program Office at time of submission [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Prepare draft labeling in [†] and discussion with the FDA.

3.6.4.2 [†]: During the review of the [†] by the FDA Division and by [†], AVI will respond promptly to comments. Recommendations of the FDA will be discussed and incorporated and the finalized files will be resubmitted immediately prior to [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final approved [†] to the FDA immediately prior to [†]. Copy of the draft [†] is sent to USG Program Office.

3.6.5 [†] by the FDA to US Government: Deliver [†] by the FDA, to the USG office immediately after the [†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: [†] configuration approved by the FDA will be delivered to the USG Program Office.

3.6.5.1 [†] to US Government: At the end of CLIN0004 [†] by the FDA will be shipped to the USG Program Office.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: [†] configuration approved by the FDA will be shipped to the USG Program Office.

3.6.5.2 Project Management, Operations and Oversight: Oversight of inventory and distribution will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.6 Prepare and Deliver [†] **to US Government:** AVI proposed to subcontract all manufacturing and testing of the drug substance and drug product. The company will submit full details of manufacturing packaging and testing of the drug substance and drug product without divesting intellectual property rights, and it will not be necessary to submit a [†] to FDA. The US GOVERNMENT will have the right of access to the full documentation for the [†] as agreed in the contract.

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Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: AVI will send an electronic and a paper copy of the approved [†] to the USG Program Office.

3.6.6.1 Ensure completion of [†] at CMO: The CMOs and manufacturers of some of the components of the final drug product configuration [†]. A copy of the CMO's Letter of Authorization permitting the FDA to access their confidential information in connection with the [†] will have been submitted in the [†]. AVI will endeavor to ensure that the CMO updates and maintains the conditions of the [†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: A copy of the Letter of Authorization for FDA to access the DMF information in connection with the review of the [†].

3.6.6.2 Submit Letter of Authorization for FDA review of [†] to US Government: The CMOs and manufacturers of some of the components of the final drug product configuration [†] will [†] that will be referenced by the name and address of the supplier and reference number in the [†]. A copy of the CMO's Letter of Authorization permitting the FDA to access their confidential information in connection with the [†] will have been submitted in the [†]. AVI will endeavor to ensure that the CMO updates and maintains the conditions of the [†].

Period of Work: Approximately [†] day (e.g. [†])

Deliverable: Deliver a copy of Letter of Authorization (to FDA) to USG.

3.6.6.3 Program management, operations and oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMT will be established to review progress and results.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.7 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall study are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

Period of Work: Concurrent with all CLIN0004 activities, a period of approximately [†] days (e.g. [†]).

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Deliverable: Provide contract management and financial oversight ensuring compliance.

3.6.7.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0004 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3.6.7.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Concurrent with all CLIN0004 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.6.7.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0004 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

3.6.7.4 EDMS and QA: The EDMS will have been fully implemented and routinely used to prepare, review and store documents for the [†], and regulatory and quality compliance documents. AVI will continue to store all documents in the validated EDMS and will make electronic document submissions to the FDA, as needed. AVI will train all pertinent staff on the EDMS, including Quality Assurance staff.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.6.8 Drug Substance and Drug Product Ongoing Stability Studies: Continue manufacturing assessment of stability [†] prepared in CLIN0002.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Continue assessment of stability study data (to include both drug substance and drug product).

3.6.8.1 Continue Drug Substance Stability Studies: Continue stability study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Continue assessment of drug substance stability data.

3.6.8.2 Continue Drug Product Stability Studies: Continue stability study.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Continue assessment of drug product stability data.

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Appendix B: Revised Statement of Work

3.0 CONTRACT

AVI BioPharma (AVI) Statement of Work for AVI-6003 as an effective therapeutic for Marburgvirus:

3.2 CLIN0005 Technology Development (Part 1): AVI will deliver the developmental therapeutic end item that has completed [†] clinical trials, with all the associated preclinical and regulatory requirements sufficient and in place to support its delivery. This will comprise all those activities necessary for our candidate drug product to complete the US GOVERNMENT (USG) Statement of Objectives for CLIN0005. We will complete the planning (including assessment and mitigation of risk) for manufacturing the drug supply, and execute process development to enable scale up from the current [†] batch GLP material, through a [†] batch cGMP engineering development scale, in anticipation of an ultimate [†] modular manufacturing scale; includes analytical methods development and validation ([†], drug substance) and method qualification (drug product), and development of specifications for lot release.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Drug product on which [†] clinical trials have been completed.

3.2.2 [†] Process Development and Qualification: AVI will prepare drug substance for use in subsequent [†] studies (includes the use of previously manufactured components outside this RFP to prepare drug substance). The [†] development program will improve process reproducibility and prepare for manufacturing at larger scales. AVI will investigate several steps that have shown variability [†], and examine steps that have challenges in scale-up [†]. The overall goal of drug substance development is to design a [†] process that is highly reproducible, and that can be demonstrated at [†] scale, and usable in the final manufacturing [†] scale. [†]. A stable, [†] form of the drug substance will be produced.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Design scalable processes for [†] and drug substance.

3.2.2.1 [†] Process Development and Qualification: The [†] development program is aimed at improving reproducibility and scalability, and ensuring the quality of the product. The overall goal is to design [†] process that is highly reproducible and easily scalable.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Finalization of a highly reproducible and easily scalable [†] process in preparation for manufacturing at larger scales.

3.2.2.1.1 Synthesis and Characterization of Authentics: This project will help ensure a consistent quality of product. [†]. These authentics will be used as markers in the analytical method validation to check the resolution of the methods.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Preparation of authentic impurity markers

3.2.2.1.2 [†] Small Scale Process Development: The [†] development program is aimed at improving reproducibility and scalability. It will investigate several steps that have shown [†]. The overall goal is to design a [†] process that is highly reproducible and easily scalable.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Improvement of specific steps and finalization of a highly reproducible and easily scalable [†] process.

3.2.2.1.3 Project Management, Operations and Oversight: Project management will oversee the CROs that are performing [†] process development and will also manage the in-house development effort

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.2.2 Drug Substance [†] Process Development: The drug substance [†] process development program will involve optimization of the [†] components of the manufacturing process. The overall goal is to design a highly reproducible and scalable [†] drug substance manufacturing process that can be demonstrated at an [†] and is usable in the final manufacturing [†] scale.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Demonstration of a reproducible and scalable manufacturing process for drug substance.

3.2.2.2.1 Drug Substance [†] Process Development: Development activities are to include optimization of [†] to produce a scalable synthesis process as well as optimization of current [†] process to increase efficiency of [†]. Investigation of alternative [†] methods [†] will also be conducted.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Optimization of the synthesis and [†] components of the manufacturing process.

3.2.2.2.2 Project Management, Operations and Oversight: This element entails oversight and guidance of the development activities, as well as management of technical personnel.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.3 Manufacturing for Nonclinical Studies:** [†] production will occur at [†], and will supply all the [†] needed for CLIN0005 drug substance manufacture, plus a contingency plan for any drug substance batch needing to be repeated (this is essential to ensure concordance with the timeline). Any

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excess [†] will be used during the scale up in CLIN0006. The current [†] drug substance process will be transferred to a contract manufacturing organization (CMO) accomplished in the [†] manufacture of oligomeric therapeutic drugs. The CMO will perform scaling of process to [†], plus process development and Reduction to Practice (RtP) run(s). Material for toxicology studies will be made.

** Drug Product for the [†] clinical trial has already been manufactured and is currently stored awaiting final preparations for the start of the study.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Produce drug substance for [†] studies using [†] scale drug substance process.

3.2.3.1 Manufacture [†]: This production is planned to occur at [†]. It will produce all the [†] needed for CLIN0005 drug substance manufacture plus a contingency if a drug substance batch needs to be repeated. Any excess [†] will be used during the scale up in CLIN0006.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Timely supply of [†] to support CLIN0005 drug substance development and manufacture.

3.2.3.1.1 Contract Negotiation, Material Acquisition: Finalize and sign contracts for production. Order long lead time and custom reagents to support upcoming campaign.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Contract and materials in place for [†] manufacture.

3.2.3.1.2 Manufacture [†]: Produce all the [†] needed for CLIN0005 drug substance development and manufacture.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Timely supply of [†] to support CLIN0005 drug substance development and manufacture.

3.2.3.1.3 Quality Audits and Review: Quality audits are managed by the Director of QA and scheduled in accordance with the Audit Master Schedule. Automatic audit reminders are issued by the EDMS. Auditors schedule travel to and from audits, write audit reports, provide lists of findings and make recommendations. The Director of QA oversees all operational aspects of audits, procedures connected with audits and audit reports. Audit findings, recommendations and responses are reviewed by the Director of QA, the VP of Regulatory Affairs and QA. Non-compliance issues are brought to the attention of the Chief Executive Officer (CEO), personally, by the Director of QA on a biweekly basis. In addition, a QA Unit and Compliance Report is written monthly by the Director of QA and presented to the CEO in a 1:1 meeting. Functional management and staffing of the QA Unit is the responsibility of, and managed by, the VP of Regulatory Affairs and QA.

Quality Audits include non-cGMP, non-GLP, cGMP or GLP audits, depending on the process step and may include audits of non-regulated facilities (non-cGMP and non-GLP facilities) or audits of facilities

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that are required to comply with cGMP or GLP. These are Direct Impact audits of Contract Manufacturing Organizations (CMOs), quality control testing, storage and distribution facilities connected with the manufacture of [†] and activated tails. Audit documentation includes a list of questions directly suited to the service provided by the CMO and an ICH Q7-compliant audit checklist. All CMOs must be audited and approved by QA and, when applicable, readiness for Pre-Approval Inspection (PAI) by the FDA or other regulatory agency is evaluated at an appropriate time during an audit. Audit records have limited, controlled review access for authorized departmental and senior management staff, and are reviewed through and archived using the EDMS.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: QA approved CMO (vendor) and release of manufactured [†] for AVI-6002 program. Audit report completed and satisfactory resolution of responses to findings for CMO providing [†]. Lot release of [†] for drug substance manufacturing program in accordance with QA-approved specifications using analytical methods.

3.2.3.1.4 Project Management, Operations and Oversight: Project management will oversee the CMO that is doing the CLIN0005 production.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.3.2 Manufacture Drug Substance: Select CMO experienced in [†] synthesis of [†] drugs. Tech transfer of [†] scale process for drug substance; scale-up of process to [†], process development and RtP run(s); determine stable [†] form for drug substance.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Achieve [†] scale drug substance process and produce material for [†] studies.

3.2.3.2.1 Select and Contract CMO: CMOs capable of performing [†] synthesis have been reviewed for suitability for the API manufacture, [†], and isolation. Site visits will be performed followed by quality audits, contract negotiations, technical transfer, and Quality agreement execution.

Period of Work: Approximately [†] days from time of award (e.g. [†])

Deliverable: Selection and completion of contracts with a suitable CMO for API manufacture.

3.2.3.2.2 Manufacturing Tech Transfer at [†]**:** Production will be introduced at the current [†] scale to allow comparability of previous lots and to transfer knowledge to the new CMO. Each API will be made and purified at this scale with the objective being to produce material suitable for toxicological studies.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Demonstration of successful tech transfer of current [†] sale and production of material suitable for [†] studies

3.2.3.2.3 Process Development, Reduction to Practice at [†]: After the tech transfer campaigns, the process size will be adapted to an approximately [†] scale as part of normal development in order to produce more material suitable for [†] studies. At this point process changes may be introduced to make the process more efficient as long as the impurity profiles remain unchanged. The batch will be run cGMP in order to supply material for the QTc clinical study and pivotal animal study in CLIN0005.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Demonstration of scalability of manufacturing process to [†] scale by successful completion of RtP run(s). Holding the API until needed for fill finish. Ship material for formulation development to precede the fill/finish in CLIN0005. Supply C of A.

3.2.3.2.3.1 Reduction to Practice at [†]: Perform the large scale manufacturing run cGMP.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Holding the API until needed for fill finish. Ship material for formulation development to precede the fill/finish in CLIN0006. Supply C of A. Demonstration of scalability of manufacturing process to [†] scale by successful completion of RtP run(s). Perform using cGMP compliant documentation and testing. Holding the API until needed for fill finish. Ship material for formulation development to precede the fill/finish in CLIN0006. Supply C of A.

3.2.3.2.4 Project Management, Operations and Oversight: As part of the normal course of outsourcing production, regular team meetings will be held and updates provided. Production oversight from site visits and data review will be shared and discussed. Regular conference calls with the CMO will be established to review progress and results.

Period of Work: Approximately [†] days from time of award (e.g. [†])

Deliverable: Plan, monitor, and report overall delivery of milestones and budget

3.2.4 Develop and Validate Analytical Assays and Lot Release Specifications: Existing analytical methods will be refined and validated for each [†]. Methods for drug substance will be developed and validated to meet characterization criteria set with the FDA for release. For the drug product assays, development will utilize synergies with drug substance methods to reduce time and cost of method qualification. For both drug substance and drug product, AVI will qualify vendors, facilities and conduct audits.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Validated assays for [†] and drug substance, qualification of the drug product assays, and development of lot release specifications for [†], drug substance and drug product.

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3.2.4.1 [†] Analytical Method Development and Validation: Existing analytical methods will be refined and validated for each [†].

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited report for validated analytical methods for each [†].

3.2.4.1.1 Method Development and Validation: Methods confirming process consistency will be developed by a qualified subcontractor. Methods for assay and impurity profile will be validated to established criteria for cGMP starting materials.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited report for validated analytical methods for each [†].

3.2.4.1.2 Identify Impurities above ID Threshold: Process-critical impurities will be synthesized and included in the validation process. Markers for known impurities will be synthesized as part of the impurity profile. Chromatograms of historic lots will be generated using the refined analytical methods. A team of chemists will work on identifying and synthesizing all impurities that occur [†].

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Identification and preparation of markers for all impurities that occur above the [†].

3.2.4.1.3 Develop (Assess and Refine) Lot Release Specifications: To ensure consistent quality, a team will assess and refine all the [†] lot release specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Preparation of a lot release specification for each [†].

3.2.4.1.4 cGMP Audits: See section 3.2.3.1.3 Quality Audits and Review for general description of Quality Audits. cGMP audits are performed by experienced auditors for the Contract Manufacturing Organizations (CMOs), quality control testing and storage and distribution facilities. Audits employ a checklist approach, based on regulatory requirements and ICH Q7 guidelines, which are customized to comply with requirements for each subcontractor site and circumstance. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of cGMP and GLP subcontractors is also evaluated. Under the Quality System, batch release specifications, test methods and quality control test results, protocols for stability studies and analytical methods and study reports or data are reviewed for compliance with regulations and guidelines and approved by the Director of QA

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audit report completed and satisfactory resolution of responses to findings by subcontract laboratories testing [†] for drug substance for subsequent clinical use.

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3.2.4.1.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.4.2 Drug Substance (DS) Analytical Method Development and Validation: Drug substance analytical methods will be developed and validated to meet characterization criteria set forth by regulatory agency for release. Impurities will be isolated and identified. Subcontractors will be qualified, and audits performed, by AVI QA Unit.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited report for validated analytical methods for drug substance release.

3.2.4.2.1 Method Development and Validation: Methods, compliant with regulatory expectations, will be developed for impurity profile, assay, identity and description. Method validation will be performed by qualified vendor.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Methods for impurity profile, assay, identity and description, validated and audited report as appropriate.

3.2.4.2.2 Identify Impurities above [†]: Impurities will be identified and the identity verified by synthesis of authentic compounds. Detection level of impurities will be established.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Establish identity and detection levels of impurities.

3.2.4.2.3 Develop (Assess and Refine) Lot Release Specifications: Release specifications will be established that ensure consistency between production lots. RTP batches will be used to refine release specifications and assess the analytical method capability to meet the specification threshold according to ICH Q6A recommendations. Director of QA participates in review and approval of specifications that are compliant with cGMP and compendial requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: cGMP-compliant lot release specifications are approved for drug substance for subsequent clinical use.

3.2.4.2.4 Quality Audits and review: Documentation for drug substance (DS) analytical method development and validation will be reviewed by QA for compliance with regulatory requirements. See section 3.2.3.1.3 Quality Audits and Review and section 3.2.4.1.4 cGMP Audits. Audits occur, reports are completed and satisfactory responses are received to audit findings. Director of QA reviews and approves validation protocols and validation reports for the analytical methods.

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Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audits occur, audit reports are completed audit findings are resolved and validated analytical tests and methods are approved for drug substance.

3.2.4.2.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.4.3 Drug Product (DP) Analytical Method Development and Qualification: Drug product analytical method development and qualification will characterize phosphate buffered saline filled drug product. Method development will utilize synergies with drug substance methods to reduce time and cost of method qualification. Includes subcontractor qualification and audits by AVI QA Unit.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Qualified analytical test methods (validated assay method) that comply with the FDA's quality and regulatory requirements for release of drug product.

3.2.4.3.1 Method Development and Qualification: Methods, compliant with regulatory expectations, will be developed for impurity profile, assay, identity, and description. Method qualification will be performed by qualified vendor. A contract analytical development laboratory will be chosen, and methods for drug product analysis and release will be developed that comply with the FDA's quality and regulatory requirements.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Audited reports for qualified methods for impurity profile, identity, and description and validated method for assay.

3.2.4.3.2 Identify Impurities above ID Threshold: Impurities will be identified and the identity verified by synthesis of authentic compounds. Detection level of impurities will be established.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Establish identity and detection levels of impurities

3.2.4.3.3 Develop (Assess and Refine) Lot Release Specifications: Release specifications will be established that ensure consistency between production lots. RTP batches will be used to refine release specifications and assess the analytical method capability to meet the specification threshold according to ICH Q6A recommendations.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Lot release specification in compliance with the FDA's quality and regulatory requirements for drug product for subsequent clinical use.

3.2.4.3.4 cGMP Audits: Documentation for drug product (DP) analytical method development and validation will be reviewed by QA for compliance with regulatory requirements. See section 3.2.4.1.4 above. Audit occurs, report completed and satisfactory resolution of responses to findings by subcontract testing laboratories developing analytical methods and testing drug product for subsequent clinical use. Lot release will occur using QA-approved validated analytical methods and specifications compliant with compendia and other regulatory requirement.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Completed and QA reviewed validation reports. Audit report completed and satisfactory resolution of responses to findings by subcontract testing laboratories. Lot release tests and specifications that comply with the FDA's quality and regulatory requirements are approved by the Director of QA.

3.2.4.3.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.5 [†]: AVI will conduct [†] studies [†]. A new assay will be used for the determination of drug levels in biological matrices, and each component of the study drug will be assayed independently. The method will be validated (GLP) in plasma as is required for study protocols for pharmacokinetic analysis. An existing [†] will be transferred and validated (GLP) for the analysis of dosing solutions, over a [†]. The single dose [†] will evaluate the effect of a single dose on target organs observed. Quality Audits will be conducted on the contract research organization (CRO) and the audit records maintained by the AVI EDMS.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Completed GLP-compliant non-clinical toxicology study reports for studies in [†], including [†] reports.

3.2.5.1 [†] Method Validation: Feasibility studies have proven a [†] method acceptable for the determination of drug levels in biological matrices. Each component of the study drug is assayed independently. The method will be validated (GLP) in matrices corresponding to samples specified by study protocols for pharmacokinetic analysis [†].

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Audited final report on validated [†] method for detection of drug levels in biological matrices.

3.2.5.2 Dose Formulation Analytical Method Evaluation and Validation: An existing [†] method will be transferred and validated (GLP) for the analysis of dosing solutions. The method will be validated over a concentration range suitable for determination of concentration, homogeneity, and stability of the dose formulations for the non-clinical toxicology studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on validated method for concentration of drug levels.

3.2.5.3 [†]: The single dose [†] study will evaluate the effect of a [†]. The results will have an impact on the dosages and escalation in the [†] trial. This study requires validation of the analytical method.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.4 [†]: This study provides supportive data for the repeat dose study [†] that has been completed. Allow correlation of observed effects with exposure.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.5 [†]: In vitro study to assess the effects of the test article on [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.6 [†]: To investigate the actions of the test article/vehicle on action potential [†] methods. This study will identify potential risk of [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] study.

3.2.5.7 [†] with Long Recovery: [†]. This study will determine [†] in multidose clinical trial

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report for [†] Study with Long Recovery.

3.2.5.8 cGLP Audits: Quality Audits conducted in this arena are Direct Impact audits of our Contract Research Organizations (CRO). Audits include a list of questions directly suited to the CRO and a GLP/cGMP [†] checklist. All CROs (through audits) are approved (or rejected) by QA and audit records are maintained by the AVI EDMS. See section 3.2.3.1.3 for general description of Quality Audits.

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Audits of [†] facilities, [†] laboratories, and related study data will be conducted by experienced auditors from the Quality Unit. Audits employ a checklist approach, based on regulatory requirements (21 CFR Part 58 for GLP compliance) and ICH guidelines. The checklists are customized to comply with requirements applicable for each subcontractor facility and type of testing. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of GLP subcontractors is also evaluated.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit report completed and acceptable responses to findings received from subcontract [†] facilities and [†] laboratories testing AVI-6002 for [†]. GLP studies will occur using QA-approved protocols that meet regulatory and IUCAC and USG requirements and validated [†] methods are used.

3.2.5.9 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.2.6 Pilot [†] **Studies:** [†] (includes 3.2.6.1 and 3.2.6.2).

3.2.6.3 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

3.2.7 Contract Program Management:** AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall study are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

** Work will continue during period [†] on this program – namely [†] and regulatory to prepare for [†] clinical study. Program management will be required to oversee those tasks.

Period of Work: Concurrent with all CLIN0005 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.2.7.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0005 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3.2.7.2 Finance and [†]: Track financial work process and reporting.

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Period of Work: Concurrent with all CLIN0005 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.2.7.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0005 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance

3.2.7.4 EDMS Installation, Validation, Implementation, Training and QA: AVI will implement enhancements to the Quality Systems Approach already in place, including installation of a secure 21CFR Part 11 compliant EDMS and preparation for electronic document submission to the FDA. AVI will train all pertinent staff on EDMS and Quality Assurance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system will have been selected, installed and fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.3 CLIN0005 Technology Development – [†] Clinical Study (Part 2): Using the currently filed IND, and [†] data obtained subsequently, AVI will establish agreement with the FDA for the acceptable protocol** [†], such as [†] review and approval. AVI will conduct and report the [†] clinical study in healthy [†].

** Discussions with the FDA are planned for [†] which will cover the [†] and additional input to the proposed [†] study may be requested.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Final study report for [†] clinical study agreed upon by the government.

3.3.1 Support [†] Submission: An [†] cannot be granted until the appropriate legislative order has been given by Congress, however, AVI will submit a Request for Consideration for an [†] and briefing document (per Section 564(c) of the FD&C Act), amendments under Project Bioshield Act of 2004, and draft FDA Guideline of June 2005. The Request for Consideration will contain data from all available research and nonclinical studies together with draft protocol synopses for the [†] studies and the first clinical study. The FDA will be asked to provide advice on the additional requirements to achieve an [†].

As requested by the FDA in the meeting, AVI will continue to submit additional scientific, [†] and [†] study data in final study reports as [†] when the final reports are available with the intention of fulfilling all requirements for an [†] before such use is required.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

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Deliverable: Letter to the FDA requesting a meeting to discuss the Request for Consideration as an [†] and Briefing Document submitted as an [†]. In addition, after the meeting with the FDA the company's notes of the meeting with the FDA will be submitted as an [†].

3.3.1.1 Support [†] Submission, Meeting with FDA and USG: AVI's regulatory affairs staff will prepare the Meeting Request Letter and Briefing Document for the Request for Consideration as an [†] Meeting with the FDA and submit them as [†]. After the Meeting with the FDA, AVI's regulatory affairs staff will prepare notes of the meeting and submit them as an [†]. The Request for Consideration as an [†] submission will be planned, prepared and managed by AVI's regulatory affairs staff, using FDA compliant electronic templates, e-publishing techniques and the EDMS. Meeting arrangements and follow-up Meeting Minutes will also be prepared and managed by RA. Oversight will be provided by AVI's senior management.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Letter to the FDA requesting a meeting to discuss a Request for Consideration as an [†] and Briefing Document submitted as an [†]. After the meeting with the FDA the company's notes of the [†] with the FDA will be submitted as an [†].

3.3.1.2 Project Management, Operations and Oversight: Consideration as an [†] request managed by AVI regulatory affairs, using FDA compliant electronic templates, electronic document management and e-submission. Meeting arrangements and follow-up meeting minutes also managed by RA. Oversight is provided by AVI's senior management.

Period of Work: Approximately [†] days from meeting date being offered with FDA (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones to timeline and budget.

3.3.2 [†] **Clinical Study:** The [†] will be conducted with [†] to this award. The timeline will not allow AVI to wait for full manufacturing scale [†] cGMP drug product material, however the drug product used will be comparable and the assay method validated. The study and discussions with the FDA will be based on the IND already opened for drug product. Dosing will start at the [†]. Based on the pharmacokinetics, safety and general tolerability, [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] clinical study report; study conducted with research scale cGMP drug product.

3.3.2.1 Clinical Site and Local Laboratory Activities: The study will be planned and executed at an audited, selected [†] Clinical Research Facility with support from a fully CLIA accredited laboratory. From initiation onward the site(s) will be monitored through to study completion and site close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

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Final report describing [†] clinical study conducted with research scale cGMP drug product manufactured at a cGMP-compliant facility.

3.3.2.1.1 Contracts and Budget: Contract and budget will be negotiated and agreed with the [†] CRO and supporting laboratories.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All contracts (site and laboratories) to permit study to be executed are agreed and signed.

3.3.2.1.2 Final Protocol to FDA; [†] submissions: Final [†] protocol submitted to FDA, [†]; feedback received and incorporated prior to study initiation.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All approvals received before initiation of clinical study.

3.3.2.1.3 Single Administration Dosing: The study will be planned and executed at an audited, selected [†] Clinical Research Facility. Site will be involved with review of study specific documentation and trained prior to first subject first visit. All interactions with site will be documented. Regular site monitoring will be planned and documented to ensure data has been verified and entered in a timely fashion, while ensuring subject safety. Any compliance issues will be raised to the clinical team for response.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] clinical study conducted under cGCP and completed on schedule, within budget.

3.3.2.1.4 Site Close Out: After completion of the last subject last visit, all data queries will be completed by the site and/or laboratory, previously validated database locked, analyses run, and draft study report prepared. In parallel formal close out of the clinical site, with disposal of unused drug supplies and completion of all outstanding documentation will occur.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All open queries and action items associated with clinical study execution are completed and documented in a site close out visit report.

3.3.2.2 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirming that subcontractors are trained to the study and ready to perform services.

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3.3.2.2.1 [†] Method Validation: Feasibility studies have proven a [†] method acceptable for the determination of drug levels in [†] matrices. Each component of the study drug is assayed independently. The method will be validated (GLP) in matrices corresponding to samples specified by the clinical study protocol for pharmacokinetic analysis [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validated [†] assay for drug levels in [†] matrices.

3.3.2.2.2 Clinical Research Organization and Data Management: The CRO is key to study success. Their team along with AVI personnel is responsible for site start up activities, site training, and study execution, including data collection and management. The statistical support is part of the CRO. This group and Data Management will develop the plans necessary for data collection, query management, data analysis and quality checks. They will prepare reports for the [†] reviews. The final clinical study report will be written by CRO personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Executed contract between AVI and CRO.

3.3.2.2.3 Central Laboratory Services and Data Transfer: Exploratory [†] accessioning and analyses will each be conducted at a central lab facility. Data from each will be sent to data management vendor for inclusion in final study report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Laboratory data report.

3.3.2.2.4 [†]: An independent [†] will be appointed to oversee and confirm dose escalation decisions. A [†] charter will be prepared and agreed with [†] members, a contract developed and a kickoff meeting and then dose escalation meetings with open and closed sessions. Members of the [†] will be available to review safety data and confirm or reject dose escalation to the next higher dose.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Decision to dose escalate continue or stop study as documented in meeting minutes.

3.3.2.2.5 Provide Electronic Data Management with Access to US Government: Enable [†] web portal with secure access to assigned study, company, vendor and USG personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Functional secure EDC portal access.

3.3.2.2.6 Drug Warehousing and Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.3.2.3 Study Documents for Clinical Sites and Final Study Report: The Clinical Research Organization (CRO) is responsible for preparing and providing to AVI for review all appropriate study specific documents, except the clinical protocol. Upon AVI authorization the CRO will send these documents to the sites in preparation for study start. Additionally, should any unexpected or serious safety events be reported, the CRO will document, discuss with AVI medical monitor, and complete the appropriate forms. At the study end, the CRO will prepare the tables, listings and figures and draft the final study report which will then be finalized with AVI input.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.3.2.3.1 Prepare and Distribute Study Documents: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], safety reporting, and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All study related documents including but not limited to: study plan and timeline, eCRF completion guidelines, monitoring reports, protocol compliance tracking, communication plan, meeting minutes, training materials and logs, drug accountability logs and final study report.

3.3.2.3.2 Final Study Report: Prepare compliant and complete final clinical study report

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Submission ready final clinical study report.

3.3.2.4 Regulatory Submissions and Templates: The near final draft clinical protocol, FDA Form 1571, FDA Form 3674, FDA Form 1572, information on the investigators (including a copy of the CV of the Principal Investigator), study facility, and [†] will be submitted as an [†] for review by the FDA. An electronic template that is compliant with electronic submission requirements will be used for the protocol. Other "Essential Documents" specified by the ICH guideline on Good Clinical Practice and 21 CFR will be collected and reviewed for compliance. The clinical study will be registered on www.Clinicaltrials.gov or an equivalent public access database.

Period of Work: Approximately [†] days from start of collection of "Essential Documents" to notification from the FDA that it is "Safe to Proceed" (not including IRB reviews and approvals) (e.g. [†]).

Deliverable: FDA Letter confirming that it is "Safe to Proceed" with the clinical study.

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3.3.2.5 GCP Audits: Clinical data and document quality checks are carried out by clinical monitors during routine monitoring of each clinical study, as required under GCP. See section 3.2.1.3 for general description of quality Audits and Review. Quality Audits performed by experienced auditors from the QA Unit at clinical investigational sites (hospitals, etc.) are Direct Impact audits that will be specifically designed to verify compliance with GCP requirements and local and international regulatory regulations and guidelines. Audits will include contractor site selection audit, study audits during the study and an end of study audit. Audit documentation will be managed and archived in the EDMS

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit report are completed and satisfactory responses to audit findings are received from CRO's clinical facilities and [†] laboratories testing drug product in clinical studies. GCP-compliant clinical studies will occur using QA-approved protocols that meet regulatory and Institutional Review Board, HIPAA and USG requirements. Validated [†] methods are used for testing clinical samples.

3.3.2.6 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.3 Store Drug Product from Clinical Lot for 2 Years Past End of Study: Samples from the drug product batches used in the [†] clinical study will be stored under specified controlled storage conditions for 2 years past the completion of the study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Store samples of drug product used in [†] clinical study.

3.3.3.1 Initiate Drug Product Storage at Drug Distributor Warehouse: Drug product from the clinical trial will be retained for at least 2 years past the end of the clinical study end. These samples will be held at the recommended storage temperature in a secured refrigerated unit that is calibrated and monitored.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Store samples of drug product used in [†] clinical study

3.3.3.2 cGMP Audits: See section 3.2.3.1.3 Quality Audits and Review for general description of quality audits and section 3.2.4.1.4 for description of cGMP audits. Audits occur, audit reports are completed and satisfactory responses to audit findings are received from the subcontract facility storing

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and distributing AVI-6002 drug product for subsequent clinical use. Release and shipping of clinical supplies to clinical facilities will occur using QA-approved procedures that are compliant with GCP and local and international regulatory requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit report are completed and satisfactory responses to audit findings are received from the CMO drug product storage facility and conditions are acceptable for drug product lots for subsequent distribution for clinical use.

3.3.4. Stability Studies: Samples from the [†] (drug substance and drug product) and [†] scale (drug substance), will be placed on a stability study at recommended storage temperature and an elevated temperature as per ICH guidelines for a minimum of [†] consistent with the RFP. A final stability report will be written by the Contract organization that performs the stability studies.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Samples of drug substance and drug product set up for [†] stability studies.

3.3.4.1 Contract Analytical Lab, Method Transfer, Short Term Stability of Drug Product at Dilutions for Clinical Study: Identify infusion sets, short term stability for at least [†].

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Report on short term stability of drug product under conditions of clinical study.

3.3.4.2 Contract and Initiate [†]: These studies will confirm the stability of the regular [†]. These studies are expected to confirm result from previous stability studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Ongoing stability studies of [†].

3.3.4.3 Refine Stability Indicating Analytical Methods for Drug Substance and Drug Product: Forced degradation studies will identify degradants using HPLC/mass spectrometry. Once peak retention times are matched to degradant/impurity ID, stability program will utilize validated HPLC methods.

Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Completion of analytical method development for Drug Substance and Drug Product.

3.3.4.4 24 Months Stability Studies Drug Product: Drug substance and the resultant drug product will be placed on a stability study at recommended storage temperature and an elevated temperature as per ICH guidelines for a minimum of [†] consistent with the RFP. This is applicable to cGMP materials made at both the [†] scales. A final stability report will be written by the Contract organization that performs the stability studies.

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Period of Work: Approximately [†] days from time of award (e.g. [†]).

Deliverable: Ongoing [†] study with drug product prepared for [†] clinical study in CLIN0005.

3.3.4.5 Ongoing Quality Audits and Review including [†] Stability Programs: Drug substance and the resultant drug product will be placed on a stability study at recommended storage temperature and an elevated temperature as per ICH guidelines for a minimum of [†] consistent with the RFP. This is applicable to cGMP materials made at both the [†] scales. A final stability report will be written by the Contract organization that performs the stability studies See section 3.2.3.1.3 Quality Audits and Review for a general description of quality audits and section 3.2.4.1.4 for a description of cGMP audits. cGMP audits occur, reports are completed and satisfactory responses to audit findings are received from subcontract laboratories conducting stability studies. Analytical testing occurs using QA-approved validated analytical methods and stability specifications compliant with compendia and other regulatory requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit report completed and satisfactory responses to audit findings received. Stability data are reported at regular intervals and reviewed by AVI.

3.3.4.6 Program Management, Operations and Oversight including [†] Stability Programs:

Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress. As part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a [†] basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.5 End of [†] FDA Meeting: AVI will request an End of [†] Meeting to discuss the future development plan including design of the [†] and the application of the [†] as soon as the data from the first clinical study is available, and appropriate questions of the agency can be formulated to enable the further clinical development. Agreement will be sought on fixed dose combination drug products, toxicology, toxicokinetics, clinical and pharmaceutical development of the drug substance and drug product, [†] development and review, with advanced notification of USG Program Office. The scheduling will depend on FDA, but the meeting should occur within 75 days of the formal request, and the briefing book will be sent to the FDA, at least 4 weeks ahead of the meeting. FDA feedback will be incorporated into the subsequent development plans. AVI's regulatory affairs staff will plan, prepare and compile the submission documents using electronic templates and e-publishing techniques; documents will be managed and stored electronically using the EDMS.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: AVI submits an End of [†] Meeting Request Letter and Briefing Document to the FDA, participates in the meeting with FDA and prepares meeting notes. AVI reviews the FDA's official Meeting Minutes to assure that key elements of the discussions and agreements reached are documented. The FDA's requirements and expectations for the appropriate regulatory procedural enhancements leading to a potential [†] are clear.

3.3.5.1 [†] FDA Meeting Request [†], Preparation of Briefing Documents: Just before the completion of [†], AVI's regulatory affairs staff will manage, prepare and compile the [†] Meeting Request Letter and Briefing Document, with key components being provided by the research and development staff and subcontractors. The submission will be prepared using electronic templates, published using e-publishing techniques and all documents will be managed and controlled in the EDMS. The [†] Meeting will be planned and held, then AVI will prepare Meeting Notes that will be submitted to the FDA. The FDA's official Meeting Minutes will be reviewed for clarity and agreement with AVI's understanding of the outcomes. As necessary, AVI will continue proactive dialogue with the FDA by mutually convenient means.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] Meeting Request Letter and Briefing Document submitted to the FDA. A meeting date is agreed and the meeting (with participation of appropriate USG representatives) is planned.

3.3.5.2 FDA Meeting, Minutes, Follow up: AVI and USG representatives will attend the End of [†] Meeting. Agreement will be sought on a variety of development and regulatory procedural topics including for example applicability of fixed dose combination drug product requirements, toxicology, toxicokinetics, clinical and pharmaceutical development of the drug substance and drug product, [†] development and review FDA feedback will be incorporated into the subsequent development plans.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The [†] Meeting with the FDA occurs. AVI's Meeting Notes and the FDA's Meeting Minutes are prepared and reflect mutual agreements and understandings of the requirements for further development and the applicable regulatory procedures.

3.3.5.3 [†] **FDA Meeting (CMC-focused):** AVI will request a [†] Meeting to discuss the future development plan, specifically the approach for [†]. Agreement will be sought on [†], with advanced notification of USG Program Office. The scheduling will depend on FDA, but the meeting should occur within [†] of the formal request, and the briefing book will be sent to the FDA, at least [†] ahead of the meeting. FDA feedback will be incorporated into the subsequent development plans. AVI's regulatory affairs staff will plan, prepare and compile the submission documents using electronic templates and e-publishing techniques; documents will be managed and stored electronically using the EDMS.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: AVI submits a [†] Meeting Request Letter and Briefing Document to the FDA, participates in the meeting with FDA and prepares meeting notes. AVI reviews the FDA's official Meeting Minutes to assure that key elements of the discussions and agreements reached are documented. The FDA's requirements and expectations for the appropriate approach to [†], leading to a potential [†] are clear.

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3.3.6 Complete [†] Clinical Trial and [†]: AVI will complete a [†] study to assess safety, tolerability and pharmacokinetics in [†] (RFP 3.3.2). The results from this first clinical study will be submitted to FDA as a supplement to the IND as soon as the data is available and the appropriate study reports are prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct and complete [†] clinical trial Submission of an [†] containing the Final Study Report of the [†] Clinical Trial and other [†] as needed to support continuing nonclinical, pharmaceutical and clinical research and development.

3.3.6.1 Prepare for and Meet with FDA to Discuss [†]: Due to the complexity and uncertainty about the FDA's expectations and requirements for [†] approval using the [†], AVI's regulatory affairs group will plan, request and manage a specific, [†] Meeting with the FDA and other interested USG agencies to discuss the application of the [†]. A Meeting Request Letter and Briefing Document will be prepared and submitted at least 4 weeks ahead of the meeting. AVI will prepare Meeting Notes and will review the FDA's official Meeting Minutes to assure agreement on the issues discussed. If necessary, further clarifications may be requested in writing. AVI will continue an open dialogue with the FDA and USG agencies involved and document those discussions.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Meeting Request and Briefing Document, attendance at the [†] Meeting, AVI's Meeting Notes and FDA's official Meeting Minutes. Agreement with the FDA and USG agencies regarding the applicability and requirements for developing oligomeric drug products under the [†], and for [†] approval.

3.3.6.2 Prepare and Submit [†] and [†]: AVI will submit [†] containing appropriate research and development data to the FDA and provide notifications to USG Program Office The agreement of the FDA will be sought to submit the protocols for the [†] studies as well as the [†] safety study for [†] and the relevant protocols will be submitted. AVI's regulatory affairs staff will plan, prepare and manage all submissions as electronic documents using electronic templates, e-publishing techniques and the EDMS.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: [†] will be submitted as [†] and the FDA's review comments will be incorporated before finalizing study protocols. [†] will be submitted as research and development data reports are available in order to keep the IND as current as possible. Copies of major submissions and correspondence will be forwarded to USG, as required.

3.3.6.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally.

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This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.7 Deliver [†] of Clinical Material to US Government: A sample of the drug product used in the [†] clinical study will be provided to the USG.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Deliver sample drug product used in [†] clinical safety study to USG.

3.3.7.1 Ship [†] to US Government: At the end of CLIN0005 at least [†] of the drug product(s) will be delivered to the recipient specified by the USG.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] clinical safety study to USG.

3.3.7.2 Project Management, Operations and Oversight: Oversight of inventory and distribution will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

CLIN0005 Final Contract Modification: Move several W9113M-10-C-0056 contract tasks originally scheduled to occur in CLIN0006 into the schedule of CLIN0005 in order to provide TMT management with nonclinical and clinical data sufficient in scope and content to justify moving to a "Milestone B" TRL-7 acquisition status and a total product commitment effort.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient nonclinical and clinical data to justify moving to a "Milestone B" TRL-7 acquisition status and a total product commitment effort.

3.3.8. Refine [†]: The critical goal of these studies is to obtain concurrence with FDA on the [†] study to be conducted under the [†]. Critical viral parameters will be addressed in PK/PD studies of [†], and in monitoring [†], both conducted at USAMRIID. The correlation of the [†] from natural infections, will guide the format and goals of the [†] study. The [†] study will be discussed and refined with the FDA. AVI will submit the protocols for the [†] prior to subcontracting the studies to USAMRIID (the proposed vendor to be pre-qualified as acceptable for GLP-compliant studies). The final protocols and final study reports will be submitted to FDA as [†].

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Establish model for [†] Studies with FDA.

3.3.8.1 Viral Time Course in [†]: – Arm 1, Single Versus Combination Agent Confirmation Study: This study is designed to evaluate and compare the post exposure prophylactic efficacy of AVI-6003 (the combined therapeutic of AVI-7287 and AVI-7288 phosphorodiamidate morpholino oligomer (PMO)) administered once daily, with a once daily therapy with single component AVI-6003 (AVI-7288 alone) in mediating survival following infection with MARV in [†] to confirm that removal of one of the components does not affect efficacy.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report confirming the results of removal of one of the components of AVI-6003 on survival of Marburg infection in [†].

3.3.8.2 [†]: This study has multiple objectives, all of which will help determine how to scale for an appropriate dose in humans. The objectives are as follows: 1) To determine influence of viral infection on the [†] of AVI-6003 to determine potential [†] in infected humans. 2) To determine the relationship between tissue drug levels and virus load (perhaps relationship to viral protein expression – Flow FISH). 3) Single dose [†] studies in [†] to inform scaling of dose in future [†] study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report containing [†].

3.3.8.3 Delayed Time to Treatment in [†]: To determine the effect of delaying treatment initiation on viremia and survival in [†] infected with Marburg Musokee virus. This study is being moved forward to better address the customer's request for a drug that can be administered [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report containing the survival of [†] in the delayed time to treatment efficacy study.

3.3.8.4 Viral Time Course in [†]: Protocol development for this study designed to satisfy multiple questions regarding the effect of varying drug dosing regimens and viral and drug distribution during an active infection.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final protocol optimizing the dose regimen and detailing the viral time course of Marburg infection in [†].

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3.3.8.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.9 Phase 2 Multidose Dose Escalation Clinical Study: A [†] Volunteers. A goal for this study is to establish a [†], the intended therapeutic schedule. [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete Phase 2 clinical study and issue final clinical study report.

3.3.9.1 Protocol [†] Approval: Full [†] in parallel; AVI will answer any questions and amend protocol if necessary. The Amended protocol will be submitted to the [†] for approval prior to and notification of site(s) start study. All required information about the investigator, site, testing laboratories and CRO responsibilities will be submitted to the FDA prior to study start at any site.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA, Ethics Committee and [†] approvals received before study start.

3.3.9.2 Clinical Site and Local Laboratory Activities: The study will be planned and executed at audited, selected [†] Clinical Research site(s) with support from selected, fully [†] accredited laboratory. Site and laboratory will have had satisfactory GCP/GLP audits and then site will be initiated, monitored through to study completion and close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

3.3.9.3 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and necessary reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Training records, meeting minutes confirm that subcontractors are trained to the study and ready to perform services.

3.3.9.4 Provide Documents to Clinical Sites and Complete Study Reports: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.3.9.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.10 Conduct Nonclinical Studies: Nonclinical [†] completed to-date in CLIN0005 include [†].[†] studies and both the [†] studies are in progress. All of the above mentioned studies were originally included in the planned studies for CLIN0005 and all are completed or on schedule according to the baseline scheduled represented in the IMS.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited Final Reports provided from CROs.

3.3.10.1 Protein Binding: Determine the interactions and binding characteristics of the individual components of AVI-6003 with plasma proteins for [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited Final Report provided from CRO.

3.3.10.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.3.11 Drug Manufacturing, Warehousing & Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.3.11.1 Drug Warehousing & Distribution – [†]: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.3.11.2 GLP Manufacturing – Refine Animal Models: Manufacture of GLP material for the animal studies.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide GLP material on time to site(s) and keep adequate records.

3.3.11.3 GMP Manufacturing at CMO – [†]: Manufacture of GMP material for the [†] clinical studies.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide GMP material on time to site(s) and keep adequate records.

3.3.11.4: GMP manufacturing of drug product at CMO – fill finish. Manufacturing of each agent is performed at CMO qualified to perform fill finish of these materials.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Provide vialed material. Ship to drug distribution and warehouse site. Provide C of A.

3.3.11.5 Perform [†] for Drug Product for [†] and [†]. AVI will contract with a CRO to develop a [†] of the drug product that will [†]. Drug substance will need to be supplied and dependent upon the quantity needed this will either be manufactured in-house or at a CMO. This development will occur on [†] in its entirety and knowledge learned from that development will be applied to the other [†] In this way only the development costs of one DP will be realized in CLIN0005/0005 while the balance of the development will occur in CLIN0006/0006 if awarded. Previous experience in [†] The development will consist of: 1. Transfer of analytical methods to development lab; 2. Thermal characterization of the current formulation; 3. Assess the need for additional excipients; 4. Optimization of the lyophilization cycle; 5. Assess the compatibility of the solution with in-process equipment; 6. Filter validation; 6. Stability studies.

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Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Development Reports.

3.3.11.6 **Transfer Analytical Methods:** The [†] for quantifying API concentration and stability assessment will be transferred to the CRO. This will include supporting the CRO with reference solutions and materials to enable them to provide product assessment during the development

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Tech transfer report.

3.3.11.7 Product characterization and [†]: Drug substance product characteristics will be determined including differential [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†], report.

3.3.11.8 Optimization of [†] Cycle: From the preliminary formulation studies the two best candidates will undergo [†] and these studies will be thoroughly evaluated for [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†], report.

3.3.11.9 Accelerated Stability Studies Leading to Selection of [†] Drug Product Formulation: [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†] formulation.

3.3.11.10 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.12 Quality Audits: The AVI Quality Management System provides for the quality oversight of the GMP, GLP and GCP work associated with this program. Subcontractors performing regulated work are audited as part of AVI's vendor qualification process. Quality audits are managed by the Director of QA and scheduled in accordance with the Audit Master Schedule. Auditors schedule travel to and from audits, write audit reports, provide lists of findings and make recommendations. Audit findings, recommendations and responses are reviewed by the Director of QA,

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the VP of Regulatory Affairs and QA, and the appropriate functional area management. Non-compliance issues are brought to the attention of the Chief Executive Officer (CEO). In addition, a QA Unit and Compliance Report will be written monthly by the Director of QA. Audits will be conducted by experienced auditors from the Quality Unit. Audits employ a checklist approach, based on regulatory requirements and ICH guidelines; the checklists are customized to address the quality and regulatory requirements for each subcontractor facility and type of testing. When applicable, the readiness for a Pre-Approval Inspection by the FDA or other regulatory agency (PAI) of subcontractors is also evaluated.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings.

3.3.12.1 Quality Audits – Facility for Animal Model Studies: Quality Audits of specialized Testing Facilities are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of on-site Direct Impact audits of the Testing Facility associated with performance of animal model studies in the BSL-4 laboratory. These are annual facility audits for the purpose of evaluating status and efforts towards GLP compliance, and for assuring that the level of compliance is appropriate to the work being performed. This task also includes annual facility audits of the CRO responsible for [†]. Audit Reports are prepared and circulated for internal review, then sent to the Testing Facility for review and response to any audit findings. Audits are closed out upon satisfactory resolution of any issues. Audit Certificates are prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings

3.3.12.2 Quality Audits – Facility for Nonclinical Studies: Quality Audits of Contract Research Organizations are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of an on-site Direct Impact facility audit of the CRO associated with performance of the planned nonclinical protein binding studies. An Audit Report is prepared and circulated for internal review, then send to the CRO for review and response to any audit findings. The audit is closed out upon satisfactory resolution of any issues. An Audit Certificate is prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings.

3.3.12.3 GCP Audits – [†]**:** Quality Audits of Contract Research Organizations are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of an on-site Direct Impact audit of the CRO associated with management of the [†]. It may be a qualification audit of a new CRO or a re-audit of a previously qualified CRO. An Audit Report is prepared and circulated for internal review, then send to the CRO for review and response to any audit findings. The audit is closed out upon satisfactory resolution of any issues. An Audit Certificate is prepared.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CRO.

3.3.12.4 GMP Audits – CMOs: Quality Audits of Contract Manufacturing Organizations are scheduled in accordance with the Audit Master Schedule as part of AVI's vendor qualification process. This task includes the performance of Direct Impact qualification audits or re-audits of contract manufacturers of [†]. Note that a Quality Audit will be conducted of a CMO's first [†] run. It will include observation of the manufacturing process per cGMP/Q7 guidelines and will be documented with a report that will be added to the initial CMO audit report. Additional GMP audits include audits of those contract organizations associated with analytical method development and validations, and lot release and stability testing. It also includes audits of CMO associated with [†]. The audits may be a facility or process audit, performed on-site or by questionnaire, as appropriate. Audit Reports are prepared and circulated for internal review, then sent to the CMO for review and response to any audit findings. Audits are closed out upon satisfactory resolution of any issues. Audit Certificates are prepared.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMO.

3.3.13 Quality Document Review: Quality Assurance review of documents (such as protocols and study reports).

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol or batch record) or for finalization of deliverables for other functional areas (e.g. study reports). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing.

3.3.13.1 Document Review – Animal Model Studies: Quality Assurance review of documents (such as protocols and study reports) associated with animal model studies and [†] testing. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol) or for finalization of deliverables (e.g. study reports).

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3.3.13.2 Document Review – Nonclinical Studies: Quality Assurance review of documents (such as protocols and study reports) associated with nonclinical protein binding studies. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol or batch record) or for finalization of deliverables for other functional areas (e.g. study reports). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing.

3.3.13.3 Document Review – [†]: Quality Assurance review of documents (protocol, GCP audit schedule, study report, etc.) associated with the [†] Clinical Study. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol or investigator brochure) or for finalization of deliverables (e.g. study reports).

3.3.13.4 Document Review – CMOs: Quality Assurance review of documents associated with manufacturing operations, performed at contract organizations, or in-house. This task also includes review of documents associated with characterization of material for use in animal model studies and nonclinical studies, as well as documents associated with validations, material specifications, lot release testing, and stability testing of lots for clinical use. It includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. study protocol or batch record) or for finalization of deliverables (e.g. study reports, lot records, release testing). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing. Certificates of Analysis.

3.3.13.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.3.14. Regulatory Submissions: [†] Clinical Information and Nonclinical Information Amendments will be submitted as soon as study reports are available to keep the [†] up to date.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] Information Amendments submitted to the FDA.

3.3.14.1 Protocols to FDA for Approval – Refine Animal Model: Protocol submitted to the FDA as an [†] amendment.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA approved protocol before initial dose of investigational material is administered.

3.3.14.2 Protocols to FDA for Approval – [†]: Protocol submitted to the FDA as an [†] amendment.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: FDA approved protocol before initial dose of investigational material is administered.

3.3.14.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track compliance, report progress. Project progress and any issues relative to the development plan will be documented and addressed with the Product Development Team on at least a monthly basis.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Develop timeline, manage vendors, anticipate and resolve problems, track compliance, report progress. Project progress and any issues relative to the development plan will be documented and addressed with the Product Development Team on at least a monthly basis.

3.3.15 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall program are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.3.15.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

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3.3.15.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.3.15.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

3.3.16.1 Subunit Process Development and Qualification: The GMP production of [†] will be examined with a focus on improving the repeatability of the plant scale production process.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The development report will be delivered to the CMC archive and any resulting process improvements will be implemented at the CMOs.

3.3.16.1.1 Development of [†] GMP Production Process: The GMP production of [†] will be examined with a focus on improving the repeatability of the plant scale production process.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: The development report will be delivered to the CMC archive and any resulting process improvements will be implemented at the CMOs.

3.3.16.1.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring timely delivery of development reports.

3.3.16.2 Manufacture [†] to Support Additional Production: Oversees the production of the additional [†] required for the drug manufacture to support the new studies. It also encompasses the required storage and retest tasks.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: [†] will be provided to Manufacturing to support the planned drug production.

3.3.16.2.1 Manufacture [†] to Support Additional Production: Oversees the production of the additional [†] required for the drug manufacture to support the new studies. It also encompasses the required storage and retest tasks.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] will be provided to Manufacturing to support the planned drug production.

3.3.16.2.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring timely delivery of subunits to support the planned drug production.

3.3.16.3 Continue [†]: The continued stability on [†] has been moved from CLIN0006 to CLIN001.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] report will be delivered to the CMC archive.

3.3.16.3.1 Continue [†]: The continued stability on [†] has been moved from CLIN0006 to CLIN001.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] report will be delivered to the CMC archive.

3.3.16.3.2 Non Labor Costs Continue [†]: Subcontractor costs associated with [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: N/A

3.3.17.1 Qualification of Analytical Methods: Validation of analytical methods suitable for [†] clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Validation report

3.3.17.1.1 Qualification of Analytical Methods for Release of AVI-7287: Validation of analytical methods suitable for [†] clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validation report

3.3.17.1.2 Qualification of Analytical Methods for Release of AVI-7288: Validation of analytical methods suitable for [†] clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Validation report

3.3.17.2 QC Analysis: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.1 QC analysis of [†] AVI-7287 for [†]: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.2 QC analysis of [†] AVI-7287: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.3 QC analysis of [†] AVI-7288 for [†]: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Release Testing results.

3.3.17.2.4 QC analysis of [†] AVI-7288: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.2.5 QC support of [†] GMP: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Release Testing results.

3.3.17.3 Stability Testing on [†] lots: Analysis of [†] for the determination of pooling criteria. Analysis of final pools. Release testing of drug substance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability Testing results.

3.4 CLIN0006: AVI will deliver the developmental therapeutic end item that has achieved [†] clinical trials, based upon CLIN0005, additional prior studies and all the associated regulatory requirements sufficient and in place to support this. This will comprise all those activities necessary for our candidate product to complete the USG Statement of Objectives in CLIN0006.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug product on which [†] clinical trials have been completed.

3.4.1: Prepare Drug Product for [†] clinical study and [†]. cGMP drug product for the [†] clinical trial and [†] will be manufactured from cGMP drug substance prepared at [†] scale in CLIN0005.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Vialed, released drug product for [†] clinical study and [†]. Audit reports.

3.4.1.1: Prepare Drug Product for [†] clinical study and [†]. cGMP drug product for the [†] clinical trial and [†] will be manufactured from cGMP drug substance prepared at [†] scale in CLIN0005.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Vialed, released drug product for [†] clinical study and [†].

3.4.1.2 Quality Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated with drug product manufacture. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMO. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch record), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing). QA issues final disposition of GMP manufacturing lots upon review and approval of release testing. Certificates of Analysis.

3.4.1.3: Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.2 Develop and Validate Analytical Assays for Drug Product: AVI will complete analytical methods development and validation for drug product and finalization of specifications for lot release of drug product. The development and validation of formulated product analytical test methods utilize the analytical test methods developed and validated for therapeutic drug substance, where applicable. The addition of compendial tests and limits for sterility, to those for appearance, identification, assay and impurities will meet the regulatory requirements for lot release and for the product lots in ICH-compliant stability testing programs. The Director of QA will participate in the review and approval of analytical test methods, analytical validation protocols and reports, and drug product specifications that comply with compendia and other regulatory requirements.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete development of analytical methods, validation and specifications for drug product.

3.4.2.1 Drug Product Analytical Method Development and Validation: Drug product analytical development will exploit similarities between the drug substance and the drug product to accelerate development and minimize validation time. As with drug substance, multiple HPLC methods are required for purity identification. Includes vendor qualification, facilities and API process audits of batch records by AVI QA Unit. AVI will complete analytical methods development and validation for drug product and finalization of specifications for lot release of drug product. The addition of methods for sterility, to those for appearance, identification, assay and impurities will meet the regulatory scrutiny required for cGMP release and ICH stability.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Complete development of analytical methods for drug product, and audited validation report.

3.4.2.2 Refine Drug Product Lot Release Specification: Based upon the results from the CLIN0005 manufacturing experience product specifications for each of the drug substances and the drug product will be developed. For the individual drug substances these will be similar to those developed in CLIN0005 since [†] studies will have been based upon these specifications that were used in the IND. Refinement of the specifications will be made based upon new assay development and analysis of lots used in the [†] studies and clinical trials.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Develop specifications for each drug substance and drug product.

3.4.2.3 Quality Audits: Perform facility audits of analytical testing laboratories, and review of all documentation associated with drug product analytical assay method development and validation. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMO. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. validation protocols) or for finalization of deliverables (e.g. analytical study report). Approval of validated analytical methods.

3.4.2.4 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report progress as part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the study plan. Study progress and any issues relative to the study plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.3 Scale-up Manufacturing, Qualification and Validation of cGMP Manufacturing Process: Manufacturing goals will include scale-up of the raw material supply [†], as well as that of drug substance. Further suppliers will be qualified. AVI will initiate the development of the full manufacturing scale of [†] modular manufacturing, and initiate validation of [†]. The manufacturing facilities will be audited for compliance with cGMP and other quality and regulatory requirements by experienced auditors. The Director of QA will participate in the review and approval of process validation protocols and reports.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Drug substance for [†] clinical trials will be prepared. Release drug substance lots for [†] clinical trials manufactured using a validated process at a cGMP-compliant facility. Lots meet the AVI-approved API specification and have been tested using validated analytical methods.

3.4.3.1 [†] Manufacturing Scale-Up: As part of the scale up process the [†] manufacturing supply chain needs to be established to produce [†] on the scale required to support the intended manufacturing scale-up. The current production capacity [†] multiple manufacturers will be utilized. However, even this effort will require expansion of [†] facilities for [†] of the activated [†]. [†] are needed to be made at the [†] to support scale up activities.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Assured supply for [†] and other raw materials.

3.4.3.1.1 Contract Additional [†] Manufacturing and [†] Sites: Negotiate and sign contracts with the additional [†] manufacturing and [†] CMOs.

Period of Work: Approximately [†] days (e.g. [†]). *Assumption: This will be complete prior to the start of CLIN0006.*

Deliverable: Selection and contract finalization of additional [†] CMOs.

3.4.3.1.2 Manufacture of [†]: Complete tech transfer with all new CMOs. Scale-up the [†] production process and manufacture the required [†] to support the drug substance manufacture.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Timely supply of [†] to support drug substance manufacture.

3.4.3.1.3 [†] Storage and Retest: Continue maintenance of purified activated [†] in commercial cGMP storage facility. Perform analytical testing prior to use if retest date has been reached.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] ready for API manufacture when needed.

3.4.3.1.4 Quality Audits and Review: Perform facility audits of CMOs, analytical testing laboratories, and storage facilities, as well as review of all documentation associated with [†] manufacture, testing and storage. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records, testing plans), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing).

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3.4.3.1.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project plan compliance, report progress. Progress and any issues will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.3.2 Manufacturing Scale-Up, Large Scale Manufacturing and Validation: The API production process will be scaled from the [†] to [†]. The drug substance process will undergo process validation in which [†] lots of drug substance are made. The scales for validation will include the [†] and the [†] scale. All validation lots will be placed on stability. Material from the validation lots will be used to manufacture drug product for the [†] clinical trial. The Director of QA participates in the review and approval of process validation protocols and reports.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited validation report for large scale manufacturing at a suitably qualified CMO.

3.4.3.2.1 Finalize drug substance manufacturing process. Based on experience from the CLIN0001 [†] cGMP production run and incorporating FDA guidance from the [†] meeting, examine and finalize the critical parameters for the drug substance production process. *(Note: In the answers to TMT questions, this was labeled as SOW 3.4.3.2.2).*

Period of Work: Approximately [†] elapsed days (e.g. [†]).

Deliverable: Refined and finalized parameters for production.

3.4.3.2.2 Drug Substance Manufacturing Scale Up to [†]: From the [†] scale, the process will be increased to a [†]. The purpose of using a smaller reaction size in a larger capacity reactor is to control costs during clinical development, but enable future scale increases in already qualified equipment. This allows minimization of costs during the program and later enables production of RFP threshold quantities for commercial production. This [†] run could consist of several cycles in the solid phase synthesis process, in order to verify applicability of the process parameters at this scale.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Demonstration of [†] scale manufacturing process.

3.4.3.2.3 Validation of cGMP Drug Substance Manufacturing Process: A process validation protocol will be written and executed under the guidance of the CMO with direct input from AVI, using guidance from the FDA from the EOP2 meeting. Results of this validation will be reviewed and, if acceptable, approved. The protocol will contain acceptance criteria in order to evaluate the success. The Director of QA participates in the review and approval of validation protocols, validation reports, and master batch records,

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited validation report for drug substance manufacturing process.

3.4.3.3 Quality Audits: Perform review of documentation associated with validation of the cGMP drug substance manufacturing process. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records, validation protocols), ongoing evaluation of processes, or for finalization of deliverables (e.g. validation reports).

3.4.3.4: Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.4 Refine and Select Drug Product Formulation: AVI will continue to develop a [†] of the drug product that will enhance the [†] based upon product characteristics learned in CLIN0005. Drug substance will need to be supplied and dependent upon the quantity needed this will either be manufactured in-house or at a CMO. Knowledge learned from prior development will be applied to the USG contracted drug products. Previous experience in [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Decision on final formulation for drug product formulation.

3.4.4.1 Transfer Analytical Methods: The [†] method for quantifying API concentration and stability assessment will be transferred to the CRO. This will include supporting the CRO with reference solutions and materials to enable them to provide product assessment during the development.

Period of Work: Approximately [†] elapsed days (e.g. [†]).

Deliverable: Tech transfer report.

3.4.4.2 Product characterization and [†]: Drug substance product characteristics will be determined including differential [†].

Period of Work: Approximately [†] elapsed days (e.g. [†]).

Deliverable: Data to support decision on [†], report.

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3.4.4.3 Optimization of [†]**:** From the preliminary formulation studies the two best candidates will undergo [†] and these studies will be thoroughly evaluated for [†].

Period of Work: Approximately [†] elapsed days (e.g. [†]).

Deliverable: Data to support decision on [†].

3.4.4.4 Quality Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated with drug product formulation development and new formulation drug product manufacture. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing).

3.4.4.5 Accelerated Stability Studies Leading to Selection of [†] Drug Product Formulation: Conduct stability studies at high temperature to drive final decision on [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†].

3.4.4.6 Determine Extractables and Leachables: Determine if any chemical components are extracted or leached from containers, closures, or materials used in administration of the drug.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Data to support decision on final [†].

3.4.4.7 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.5 Manufacture cGMP Material at Scale for Nonclinical and Clinical Studies and Consistency Lots: Preparation of cGMP drug product for [†] clinical safety. Three drug product batches will be validated and all will provide material for stability studies.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] scale cGMP drug product manufactured for [†].

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3.4.5.1 Drug Product Engineering Run: Drug product configuration and process will be transferred to CMO. An engineering run is planned with the first drug substance of the drug substances manufactured in CLIN0002 for the purposes of testing all fill finish capabilities including [†], formulation testing, and product testing for adherence to product specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Process suitable for GMP drug manufacture.

3.4.5.1.1 Drug Product Engineering Run: An engineering run is planned with the first drug substance of the combination product manufactured in CLIN0006 for the purposes of testing all fill finish capabilities including [†], formulation testing, and product testing for adherence to product specifications.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Process suitable for GMP drug manufacture of commercial material.

3.4.5.2 Manufacture, Release, Label 3 Consistency Lots of Drug Product: A process validation protocol will be written and executed under the guidance of the CMO with direct input from AVI, using guidance from the FDA from the [†] meeting. Material produced at scale will be filled for the clinical lots and for the consistency lots at a size commensurate with the production scale of the contract manufacturing organization.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Released, labeled drug product for clinical trials. Audited validation report for drug product manufacturing process.

3.4.5.3 cGMP Audits: Perform facility audits of contract manufacturing organizations, and review of all documentation associated with at scale drug product manufacturing and consistency lots. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. master batch records), ongoing evaluation of processes, or for finalization of deliverables (e.g. lot records, release testing).

3.4.5.4 Project Management, Operations and Oversight: The program will be managed by AVI personnel and consist of initial technology transfer and reduction to practice lots prior to cGMP production. Hands on training may be provided initially but after establishment of the process and successful manufacturing the program will be managed through conference calls, sites visits, audits, data and document review including specifications and comparison of release data with those specifications.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.6 Stability Studies: Continuing stability studies from CLIN0005 and start of [†] ICH stability studies. Drug substance and Drug product will be evaluated according to ICH stability requirements. The duration of the stability program is [†], and it will exceed the minimum requirement in the statement of objectives and Target Product Profile (TPP) threshold. The stability program includes full term aging studies at [†] will not be performed on the drug substance, but will be performed on the lyophilized drug product.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies of [†] and validated drug substance have been initiated. Stability studies set up for [†] scale cGMP drug product material manufactured for [†] safety studies.

3.4.6.1 Stability on [†] and Drug Substance ([†] Stability Program Starts): Follow ICH guideline Q1A to acquire data to justify retest date at defined storage condition.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of stability studies from CLIN0005 and initiation of studies on [†] and validated drug substance.

3.4.6.1.2 Ongoing Stability on Drug substance: This is the completion of the drug substance stability program started in CLIN0005.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug substance.

3.4.6.1.3 Stability Studies Drug Substance ([†] Stability Program Starts): Each drug substance manufactured will be placed on a [†] stability program in order to demonstrate the long term product characteristics of the material. All cGMP lots made in CLIN0002 will be placed on stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug product.

3.4.6.2 Stability on Drug Product ([†] Stability Program Starts): Follow ICH guideline Q1A to acquire data to justify expiration date at defined storage condition. All CLIN0005 cGMP drug product lots will be placed on stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug product.

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3.4.6.2.1 Drug Product Stability Studies: Drug product manufactured to supply the pivotal animal efficacy and QTc clinical studies will be placed on stability.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability data for drug product for pivotal animal efficacy and QTc clinical studies.

3.4.6.2.2 Stability Studies Drug Product ([†] Stability Program): New drug product stability studies will be set up for [†]. Multiple temperature storage conditions will be examined to provide the storage conditions for optimal use.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Initiation of stability program for drug product.

3.4.6.3 cGMP Audit: Perform facility audits of contract manufacturing organizations, and review of all documentation associated drug product stability studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. QA Document Review tasks are performed a part of the approval process for either initiation of work (e.g. stability protocols) or for finalization of deliverables (e.g. analytical study report). Audited final report on stability and shelf life of drug product.

3.4.6.4 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.7 Stability Testing to Define Operational Storage (Time Temperature Indicator): Each drug product is [†], which makes room temperature storage feasible and reduces cold chain requirements, exceeding minimum requirement in the statement of objectives and TPP threshold. The scope of the stability studies will establish the Time Temperature Indicator (TTI), since it includes full term accelerated conditions. Based upon the results, a TTI can be established to support the product shipments. As part of the operational storage and distribution criteria, product shipments will be monitored for excursions during shipment using temperature monitoring devices.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies set up for [†] scale cGMP product material to establish TTI.

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3.4.7.1 Conduct Stability Studies under [†]: These studies will be conducted at [†] temperature than the recommended storage condition to determine additional time that the material may exposed to harsher conditions without risk.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies completed to establish TTI.

3.4.7.2 Conduct Shipping and Transport Stability Studies: These studies will show that the drug product is stable under the actual conditions of shipping.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Stability studies completed to establish TTI.

3.4.7.3 Quality Audits: Stability Study Audits are Direct Impact audits. Audits include a list of questions directly suited to the supplier and a cGMP, GLP (Analytical) checklist (again dependent on supplier). All suppliers (through audits) are approved (or rejected) by QA and audit records are maintained by the AVI EDMS. The Director of QA reviews and approves stability study protocols as well as reports on stability data.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Documented audit findings. Approved stability study protocol and approved study data and reports.

3.4.7.4 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.8 Conduct Nonclinical Studies: In addition to the multiple studies completed to date and forming the basis for the open IND, the studies since then and prior to this award that will supplement that IND, AVI will also complete further [†] studies, for example [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct [†] scale cGMP product material.

3.4.8.1 [†]:[†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final Report on [†].

3.4.8.2 [†]: [†] to provide data necessary for registration.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient [†].

3.4.8.3 [†] Mass Balance: [Mass balance study required to show fate of drug in [†]; required data for registration.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report from CRO on mass balance in the [†].

3.4.8.4 [†] in vivo Metabolism: Provide data on metabolism of drug in [†] model. Required for registration and determination if any metabolites are present that need to be monitored in preclinical and clinical trials.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Final report from CRO on in vivo metabolism in the [†].

3.4.8.5 [†]: This study was moved to 3.3.10.1 as part of the contract modification.

3.4.8.6 [†] Dose Range Finding Study: To determine the effect of treatment on the [†] development, with determination of appropriate dose levels for the definitive [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on [†] study.

3.4.8.7 [†] **Study**: The definitive study to determine the effect of treatment on the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audited final report on [†] study.

3.4.8.8 Quality Audits: Perform facility audits of animal testing facilities and [†] laboratories, and review of documentation, associated with GLP toxicology studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. Quality Assurance review of documents (such as protocols and study reports).

3.4.8.9 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.9 [†] Efficacy Studies in [†]: The [†] studies will confirm therapeutic efficacy at specific dose levels and expected exposures that will be mimicked in [†]. Using the currently filed IND, clinical safety and any animal data obtained during CLIN0005, any additional preclinical data, and based on the protocol developed with FDA as to the studies necessary under the [†], AVI will conduct the [†] studies, necessary to show protection against an [†] challenge by injection.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct NHP [†] studies using [†] scale cGMP product material.

3.4.9.1 [†] Efficacy Studies in [†] #1: The [†] studies will confirm therapeutic efficacy at specific dose levels and expected exposures that will be mimicked in [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct NHP [†] studies using [†] scale AVI-6003 cGMP product material

3.4.9.1.1 [†] Acquisition and Acclimation: Prior to [†] protocols are reviewed by [†]. Once protocols are approved, [†]. [†] are held in quarantine to ensure acclimation to the laboratory setting and receive a final health evaluation. Finally, randomization and cage arrangements are finalized.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient [†] acclimated and released for first pivotal study to begin.

3.4.9.1.2 Conduct Study, Laboratory Analyses, Viral Sequencing: This is the "in-life" phase of the study involving [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of the [†] portion of the first [†] study.

3.4.9.1.3 Data Analyses, Final Study Report: Compile observations and unblind data. Statistical analysis and preparation of a final study report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Presentation of final study report.

3.4.9.2 [†] **Studies in** [†]**:** The [†] studies will confirm therapeutic efficacy at specific dose levels and expected exposures that will be mimicked in [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct NHP [†] studies using [†] scale AVI-6003 cGMP product material

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3.4.9.2.1 [†] Acquisition and Acclimation: Prior to [†] protocols are reviewed by [†]. Once protocols are approved, [†] acquisition can take place. [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Sufficient [†] acclimated and released for second pivotal study to begin.

3.4.9.2.2 Conduct Study, Laboratory Analyses, [†]: This is the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Completion of the [†] portion of the [†] study.

3.4.9.2.3 Data Analyses, Final Study Report: Compile observations and unblind data. Statistical analysis and preparation of a final study report.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Presentation of final study report.

3.4.9.3 Data Management: Full data management and statistical analysis plans will be developed by a qualified Contract Research Organization, and shared with the FDA (and USG) before studies completed. The CRO will monitor source documents (to the extent possible in a BSL4 environment), collect data, ensure all data queries are clarified, lock database, analyze and then reveal treatment allocation.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct analyses of pivotal efficacy studies for study reports.

3.4.9.4 GLP Audits: Perform facility audits of [†] testing facilities and [†] laboratories, and review of documentation, associated with [†] studies. See section 3.8.1 Quality Audits and Review for a general description of quality audits. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CMOs. Quality Assurance review of documents (such as protocols and study reports).

3.4.9.5 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project plan compliance, report progress. Progress and any issues will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

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3.4.10 Activities to Achieve Pivotal Efficacy Studies: AVI will prepare and submit [†]. The Final Protocols for the [†] studies will also be submitted after the FDA responses are received from the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: [†] submitted to the FDA.

3.4.10.1 [†] (Clinical, Nonclinical): [†] will be submitted as soon as study reports are available to keep the [†]. The Final Protocols for the [†] studies will also be submitted as [†] after the FDA responses are received from the [†].

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: [†] submitted to the FDA.

3.4.10.2 [†] (Drug Substance, Drug Product): [†] will be submitted as soon as data are available on the lots of drug substance and drug product that will be used in the [†] Studies are available. Additional [†] will be submitted as reports and data are available to keep the [†].

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Prepare and submit [†].

3.4.10.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.11 Request and Conduct [†] Meeting with the FDA: AVI will request an [†] to provide a summary of results of the [†] clinical studies and to discuss the [†] clinical development plan. The topic of designation as a [†]. A Meeting Request Letter and Briefing Document will be submitted to the FDA. Advanced notification of the meeting, plus copies of all meeting-related documents will be provided to the USG Program Office in a timely manner. After the meeting AVI's regulatory affairs staff will prepare and submit notes of the meeting as an [†]. The FDA's official Meeting Minutes will be reviewed to ensure that they reflect the same meeting outcomes and agreements as those documented by AVI.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: [†] Request and Briefing Document submitted to the FDA. Participate in [†] meeting with FDA. Prepare notes of the meeting and review the FDA's official Meeting Minutes to assure that both the FDA and AVI agree on the outcomes of the discussion and agreements.

3.4.11.1 Prepare Meeting Request and Briefing Document: The Meeting Request Letter and Briefing Document will be prepared as soon as is feasible and submitted to the FDA at least one month in advance of the requested meeting date. . Advanced notification of the meeting, plus copies of all meeting-related documents will be provided to the USG Program Office in a timely manner.

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: [†] Meeting Request Letter and Briefing Document submitted to the FDA.

3.4.11.2 [†]:[†].

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: Submit request for [†] to the FDA.

3.4.11.3 FDA Meeting, Minutes and Follow Up: AVI will attend the [†] with the FDA. AVI will submit notes of the meeting to the FDA and ensure that the company is in agreement with the outcomes and agreements recorded in the FDA's official Meeting Minutes. Clarifications will be requested, as necessary. AVI will continue an open dialogue with the FDA as development continues.

Period of Work: Approximately [†] week (e.g. [†]).

Deliverable: AVI will provide copies of the company's notes and the FDA's official Meeting Minutes to the USG Program office.

3.4.11.4 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track compliance, report progress. Project progress and any issues relative to the development plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†])

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.12 [†]:[†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] clinical safety study to USG

3.4.12.1 Ship [†] to US Government: At the end of CLIN0006 at least [†] of the drug product(s) will be delivered to the recipient specified by the US Government.

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Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] clinical safety study to USG

3.4.12.2 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.13 Phase 2 Multidose Dose Escalation Clinical Study: This study was moved to 3.3.9 as part of the contract modification.

3.4.14 [†] Clinical Study: AVI will conduct a [†]. A specialized [†], is expected to support efficient enrollment and evaluation. Subject accrual and treatment is scheduled for less than [†] months. The results will be available for the planning of the expanded [†] trial.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct [†] clinical study using [†] scale cGMP drug product material and issue final clinical study report.

3.4.14.1 Clinical Site and Local Laboratory Activities: Clinical sites and laboratories will be audited for compliance with GCP, selected and then initiated, monitored through to study completion and close out. The study will be planned and executed at audited, selected [†] Clinical Research site(s) with support from a fully [†] accredited laboratory. From initiation forward the site(s) will be monitored through to study completion and site close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

3.4.14.1.1 Contracts and Budgets: Contracts will be negotiated with vendors for the execution of this study.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Signed contracts in place with all vendors before initiation of [†] clinical study.

3.4.14.1.2 [†] Approval: Full protocol will be submitted to [†] in parallel; AVI with CRO will answer any questions and amend protocol if necessary to ensure final ethics approval, and notification of site(s) prior to study start.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All approvals received before initiation of clinical study.

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3.4.14.1.3 Site Activities First Patient in to Last Patient Out: The study will be planned and executed at an audited, selected [†] Clinical Research Facility. Site will be involved with review of study specific documentation and trained prior to first subject first visit. All interactions with the site will be documented. Regular site monitoring will be planned and documented to AVI (or Contract Research Organization staff) will monitor conduct of the [†] study to ensure data has been verified and entered in a timely fashion, while ensuring subject safety. Any compliance issues will be raised to the clinical team for response.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Complete in life portion of [†] study and complete electronic case report forms on schedule and within budget.

3.4.14.1.4 Site(s) Close Out: After completion of the last subject last visit, all data queries will be completed by the site and/or laboratory, previously validated database locked, analyses run, and draft study report prepared. In parallel formal close out of the clinical site, with disposal of unused drug supplies and completion of all outstanding documentation will occur.

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: All open queries and action items associated with clinical study execution are completed and documented in a site close out visit report.

3.4.14.2 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and necessary reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirm that subcontractors are trained to the study and ready to perform services.

3.4.14.2.1 Clinical Research Organization and Data Management: The CRO is key to study success. Their team, along with AVI personnel, is responsible for site start up activities, site training, and study execution, including data collection and management. The statistical support is part of the CRO. This group and Data Management will develop the plans necessary for data collection, query management, data analysis and quality checks. They will prepare reports for the [†] reviews. The final clinical study report will be written by CRO personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Executed contract between AVI and CRO.

3.4.14.2.2 Central Laboratory Services and Data Transfer: [†] and analyses will each be conducted at a central lab run at one facility. Data from each will be sent to data management vendor for inclusion in final study report.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Laboratory data reports provided to data management vendor.

3.4.14.2.3 [†]: An independent [†] will be appointed to oversee and confirm dose escalation decisions. A [†] charter will be prepared and agreed with [†] members, a contract developed and a kickoff meeting and then dose escalation meetings with open and closed session. Members of the [†] will be available to review safety data and confirm or reject escalation to the next higher dose.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Decisions to dose escalate, continue or stop study as documented in meeting minutes.

3.4.14.2.4 Provide Electronic Data Management with Access to US Government: Enable [†] with secure access to assigned study, company, vendor and USG personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Functional secure [†] access.

3.4.14.2.5 Drug Warehousing and Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.4.14.3 Provide Documents to Clinical Sites and Complete Study Reports: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.4.14.3.1 Prepare and Distribute Study Documents: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: All study related documents including but not limited to: study plan and timeline, [†] guidelines, monitoring reports, protocol compliance tracking, communication plan, meeting minutes, training materials and logs, drug accountability logs and final study report.

3.4.14.3.2 Final Study Report: Prepare Submission ready final clinical study report.

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Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: The Final Study Report will be submitted to the FDA as an [†]. Submit compliant and complete final clinical study report.

3.4.14.4 GCP Audits: Perform Quality Audits of Contract Research Organization and review of documentation associated with management of the [†]. See section 3.8.1 Quality Audits and Review for a general description of quality audits. Includes internal circulation of documents for functional area review.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audit and audit certificate are completed and satisfactory responses to audit findings are received from the CRO. Quality Assurance review of documents (such as the study protocol, investigator brochure, and clinical study report).

3.4.14.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.4.15 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall program are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable. In addition AVI will continue to implement enhancements to the Quality Systems Approach already in place, including installation of a secure 21 CFR Part 11 compliant EDMS and preparation for electronic submission of documents to the FDA. The EDMS will be utilized for document management and control, including collaborative authoring of study reports and eCTD text for the [†], revision and versioning control with metadata for audit trails, and secure document repository. The EDMS will provide authorized representatives of USG electronic access to program status information. The use of eCTD compliant document templates and completed reports for electronic submissions to the FDA will be managed, controlled, archived and regulated under the Quality System in the EDMS.

Period of Work: Concurrent with all CLIN0006 activities. Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.4.15.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0006 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

† DESIGNATES PORTIONS OF THIS DOCUMENT THAT HAVE BEEN OMITTED PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT FILED SEPARATELY WITH THE COMMISSION.

3.4.15.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Concurrent with all CLIN0006 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.4.15.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0006 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

3.4.15.4 EDMS and QA: AVI will continue to store all documents on the validated EDMS and preparation for electronic document submission to the FDA. AVI will train all pertinent staff on EDMS and Quality Assurance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.5 CLIN0007: AVI will deliver the developmental therapeutic end item that has achieved [†] Clinical Study, based upon CLIN0005 and CLIN0006 (recognizing that some activities will be concurrent), additional prior studies and all the associated regulatory requirements sufficient and in place to support this. This will comprise all those activities necessary for our candidate drug product to complete the USG Statement of Objectives in CLIN0003.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug product on which [†] Clinical Study has been completed.

3.5.1 Complete Pivotal Efficacy Studies: This has been moved to CLIN0006 3.4.9.1 and 3.4.9.2.

3.5.2 [†]: Continue to implement enhancements to the Quality Systems Approach already in place, including installation of a secure 21CFR Part 11 compliant EDMS and preparation for electronic submission of documents to the FDA.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Submit the quality amendment to FDA as a supplement to the AVI-6003 [†].

3.5.2.1 Write and Submit [†]: Update information stored on EDMS and preparation for electronic submission of documents to the FDA.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Submit the quality amendment to FDA as an [†].

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3.5.2.2 Respond to FDA Questions: Develop and provide response to any questions or recommendations from FDA following filing of [†].

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Submit to FDA as an [†].

3.5.2.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track protocol compliance, report project progress. As part of the normal course of conducting clinical trials, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget

3.5.3 [†] Study: Using the currently filed AVI-6003 [†], clinical safety and any [†] data obtained during CLIN0005 and CLIN0006, AVI will initiate the [†] Study in [†] using the protocols agreed with FDA, while ensuring all necessary [†] study requirements such as [†] review and approval. AVI will conduct this [†]. FDA concurrence that this will be sufficient for the safety database to [†] will be sought.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Conduct and audit [†] study and issue final study report.

3.5.3.1 Clinical Site and Local Laboratory Activities: The study will be planned and executed at audited, selected [†] Clinical Research site(s) with support from a fully [†] accredited laboratory. From initiation forward the site(s) will be monitored through to study completion and site close out.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, conduct and complete [†] clinical study. Provide all required data to the CRO for final study report.

3.5.3.1.1 Contracts and Budgets: Contracts will be negotiated with vendors for the execution of this study.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Signed contracts in place with all vendors before initiation of [†] clinical study

3.5.3.1.2 [†] Approval: Full protocol will be submitted to [†] in parallel; AVI with the CRO will answer any questions and amend protocol if necessary to ensure final ethics approval and notification of site(s) prior to study start.

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Period of Work: Approximately [†] months (e.g. [†])

Deliverable: FDA, Ethics Committee and [†] approvals received before initiation of the [†] safety study.

3.5.3.1.3 Site Activities First Patient in to Last Patient Out: The study will be planned and executed at an audited, selected clinical sites. Sites will be involved with review of study specific documentation and trained prior to first subject first visit. All interactions with the sites will be documented. Regular site monitoring will be planned and documented to AVI (or Contract Research Organization staff) will monitor conduct of the [†] study to ensure data have been verified and entered in a timely fashion, while ensuring subject safety. Any compliance issues will be raised to the clinical team for response.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Complete in life portion of pivotal safety study and complete electronic case report forms on schedule and within budget.

3.5.3.1.4 Site(s) Close Out: After completion of the last subject last visit, all data queries will be completed by the site and/or laboratory, previously validated database locked, analyses run, and draft study report prepared. In parallel formal close out of the clinical site, with disposal of unused drug supplies and completion of all outstanding documentation will occur.

Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: All open queries and action items associated with clinical study execution are completed and documented in a site close out visit report.

3.5.3.2 Outsource Services: Identify, select and qualify subcontractors needed to execute clinical study. Assigned vendor personnel will participate in a kick off meeting in which study expectations and needs, including timelines, will be discussed. Protocol and procedure training will occur. A communication plan and necessary reports will be developed prior to first subject enrolled.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Training records, meeting minutes confirm that subcontractors are trained to the study and ready to perform services.

3.5.3.2.1 Clinical Research Organization and Data Management: The CRO is key to study success. Their team, along with AVI personnel, is responsible for site start up activities, site training, and study execution, including data collection and management. The statistical support is part of the CRO. This group and Data Management will develop the plans necessary for data collection, query management, data analysis and quality checks. They will prepare reports for the [†] reviews. The final clinical study report will be written by CRO personnel.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Executed contract between AVI and CRO.

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3.5.3.2.2 Central Laboratory Services and Data Transfer: [†] and analyses will each be conducted at a central lab facility. Data from each will be sent to data management vendor for inclusion in final study report.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Laboratory data reports provided to data management vendor.

3.5.3.2.3 [†]: An independent [†] will be appointed to oversee and confirm dose escalation decisions. A [†] will be prepared and agreed with [†] members, a contract developed and a kickoff meeting and then dose escalation meetings with open and closed session. Members of the [†] will be available to review safety data and confirm or reject escalation to the next higher dose.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Provide safety oversight for pivotal safety study. Decisions to dose escalate, continue or stop study as documented in meeting minutes.

3.5.3.2.4 Provide Electronic Data Management with Access to US Government: Enable [†] with secure access to assigned study, company, vendor and USG personnel.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Functional, secure [†] access.

3.5.3.2.5 Drug Warehousing and Distribution: Store clinical trial material at refrigerated conditions in secure, temperature controlled and monitored unit. Implement traceable distribution system with chain of custody documentation.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Provide clinical trial material on time to site(s) and keep adequate records.

3.5.3.3 Provide Documents to Clinical Sites and Complete Study Reports: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study, including but not limited to: study specific data collection forms (electronic case report forms), the study operations manual, training on the protocol, clinical trial material storage, inventory and administration, use of [†], and Good Clinical Practice regulations.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Shipping receipts showing what was sent to whom and when.

3.5.3.3.1 Prepare and Distribute Study Documents: CRO, lab vendors and drug warehouse provide complete set of documents and forms to effectively and efficiently conduct study.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: All study related documents including but not limited to: study plan and timeline, eCRF completion guidelines, monitoring reports, protocol compliance tracking, communication plan, meeting minutes, training materials and logs, drug accountability logs and final study report.

3.5.3.3.2 Final Study Report: Prepare submission ready final clinical study report.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Submit compliant and complete final clinical study report.

3.5.3.4 GCP Audits: Audits will be performed of Clinical Study Sites.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Audits will occur, audit reports completed and satisfactory responses to audit findings will be required from clinical sites. Study reports and data listings will be reviewed and approved by the CRO's QA unit and by AVI's monitor and QA Unit.

3.5.3.5 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.5.4 Refine and Select Formulation and Delivery System: AVI will continue the assessment of stability for the validation lots prepared in CLIN0006. The drug kit per treatment will comprise [†]. The storage of the kit will be at room temperature (15°C to 30°C). This drug product kit meets the [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Finalize the drug kit components for drug product.

3.5.4.1 Determine Configuration for Market: All details of the commercial formulation are finalized ([†]).

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Finalize the drug kit components for AVI-6003 product.

3.5.4.2 Identify Manufacturer for Packaging Final Product: Establish contract for assembling final marketing packages.

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Finalize the vendor for manufacture, labeling and packaging of AVI-6003 product.

3.5.4.3 Continue Drug Substance and Drug Product Stability Studies: Continue drug substance and drug product stability studies.

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Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Continue stability for drug substance and drug product.

3.5.4.4 Project Management, Operations and Oversight: Track progress and manage issues as they arise.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.5.5 Deliver [†] to US Government: Deliver at least [†] of product, from the lot used for the [†] study.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] study to USG.

3.5.5.1 Deliver [†] to US Government: At the end of CLIN0003 at least [†] of the drug product(s) will be delivered to the recipient specified by the USG.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Deliver sample of drug product used in [†] study to USG

3.5.5.2 Project Management, Operations and Oversight: Oversight of inventory and distribution will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.5.6 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall program are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.5.6.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0006 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3. 5.6.2 Finance and [†]: Track financial work process and reporting.

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Period of Work: Concurrent with all CLIN0006 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.5.6.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0006 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

3.5.6.4 EDMS and QA: AVI will continue to store all documents on the validated EDMS and preparation for electronic document submission to the FDA. AVI will train all pertinent staff on EDMS and Quality Assurance.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.6 CLIN0008: AVI will deliver the FDA approved therapeutic end item including all New Drug Application and Approval activities resulting in the delivery of at least [†], based upon CLIN0005, CLIN0006 and CLIN0007 (recognizing that some activities will be concurrent), additional prior studies and all the associated regulatory requirements sufficient and in place to support this. This will comprise all those activities necessary for [†] drug product to complete the USG Statement of Objectives in CLIN0008.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Drug product approved by FDA.

3.6.1 [†] Meeting with the FDA: A [†] Meeting with the FDA will be requested and a Briefing Document submitted approximately one month in advance of the meeting. The FDA will schedule the meeting within 60 days of the request. The purpose of the [†] Meeting is to reach agreement on the electronic format and content of the [†]. The [†] will also be discussed at this meeting. AVI will prepare notes of the meeting that will document the discussion and agreements with the FDA; the notes will be submitted to the FDA. The FDA will issue official Meeting Minutes. AVI will follow up to request clarifications, as needed.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI prepares and submits Request Letter and Briefing Document, participates in the [†] meeting with the FDA, prepares notes of the meeting that are submitted to the FDA.

3.6.1.1 Prepare Meeting Request and Briefing Documents: The [†] Meeting Request Letter and Briefing document will be prepared and submitted as soon as is feasible after the completion of dosing in the clinical trials approximately [†] ahead of the meeting. Advanced notification of the meeting, plus copies of all meeting-related documents will be provided to the USG in a timely manner.

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Period of Work: Approximately [†] month (e.g. [†]).

Deliverable: AVI [†] Meeting Request Letter and Briefing Document are submitted to the FDA.

3.6.1.2 [†] Meeting, Minutes and Follow Up: AVI will participate in the [†] with FDA, take notes and obtain official minutes, following up on any action items due. AVI will provide copies of the FDA's Meeting Minutes to USG.

Period of Work: Approximately [†] weeks (e.g. [†]).

Deliverable: AVI's [†] Meeting notes and the FDA's official Meeting Minutes.

3.6.1.3 Project Management, Operations and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMT will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.2 Prepare, Submit and FDA Review of [†]: AVI will electronically submit an [†] that meets the USG's Target Product Profile. By using eligibility as a small business enterprise, and employing regulatory procedural relief benefits due [†], AVI is planning for the [†] to be prior to the completion of the contractual period proposed. During the FDA's review, AVI will remain ready to respond promptly to any questions that arise by using secure email correspondence. The USG will be kept fully informed of progress.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI prepares and electronically submits an [†] that meets the FDA's requirements for review and validation.

3.6.2.1 Complete and Submit [†] and Respond to FDA Review Comments: AVI will complete and submit an [†] to the FDA; and respond in a timely fashion to Information Requests and other comments from the FDA reviewers.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: An [†] that has been submitted electronically to the FDA and accepted for filing as an appropriately structured electronic submission. Responses to Requests for Information and the [†] from the FDA will be answered promptly.

† DESIGNATES PORTIONS OF THIS DOCUMENT THAT HAVE BEEN OMITTED PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT FILED SEPARATELY WITH THE COMMISSION.

3.6.2.2 Project Management and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.3 [†] and Response to FDA [†]: Given the issues faced by the FDA [†], it is likely that the FDA [†]. AVI will attend and participate in an ACM, and respond promptly to any questions in the [†] approval occurs.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Responses to Requests for Information from the FDA will be submitted promptly. AVI will prepare a Briefing Document and presentation materials for an [†]. Draft notes of the [†] will be prepared.

3.6.3.1 [†]: AVI will plan and prepare and, once confirmed, attend and participate at [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: AVI will prepare a presentation and Briefing Document in advance of the ACM.

3.6.3.2 Prepare and Submit Complete Response to [†]: At the conclusion of their review, the FDA will issue a [†].

Period of Work: Approximately [†] months (e.g. [†]).

Deliverable: Complete Response will be made to any questions asked by the FDA.

3.6.3.3 Project Management and Oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.3.4 [†]: AVI will receive formal confirmation [†]. AVI will submit [†] and participate in the final negotiations of the [†].

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Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Receipt of the [†]. A copy will be sent to the USG Program office.

3.6.4 [†] in Compliance with FDA Requirements: The [†]. The [†], or in the electronic format required by the FDA at that time. The [†] will have been submitted to the FDA in the [†] at that time.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Prepare [†].

3.6.4.1 Structured [†] Review and Responses: Preparation of the draft [†] (i.e. the physician's information and patient information leaflet) will be started before [†] to facilitate discussion with the FDA and information will continue to be added up [†]. Two versions are required to be submitted in the [†], one of which is annotated with the source data for each statement. Both versions are submitted electronically in the required XML format. During review by the FDA Division and by [†], AVI will respond to comments promptly. At the conclusion of the FDA review, AVI will resubmit the final version of the agreed labeling as an SPL (XML) format. [†] will be sent to the USG Program Office at time of submission [†].

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Prepare draft labeling in [†] and discussion with the FDA.

3.6.4.2 [†]: During the review of the [†] by the FDA Division and by [†], AVI will respond promptly to comments. Recommendations of the FDA will be discussed and incorporated and the finalized files will be resubmitted immediately prior to [†].

Period of Work: Approximately [†] weeks (e.g. [†]).

Deliverable: Final approved [†] to the FDA immediately prior to [†]. Copy of the draft [†] is sent to USG Program Office.

3.6.5 [†] by the FDA to US Government: Deliver [†] by the FDA, to the USG office immediately after the [†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: [†] configuration approved by the FDA will be delivered to the USG Program Office.

3.6.5.1 [†] to US Government: At the end of CLIN0004 [†] by the FDA will be shipped to the USG Program Office.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: [†] configuration approved by the FDA will be shipped to the USG Program Office.

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3.6.5.2 Project Management, Operations and Oversight: Oversight of inventory and distribution will be managed by AVI personnel through site visits, audits, and records review.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.6 Prepare and Deliver [†] to US Government: AVI proposed to subcontract all manufacturing and testing of the drug substance and drug product. The company will submit full details of manufacturing packaging and testing of the drug substance and drug product without divesting intellectual property rights, and it will not be necessary to submit a [†] to FDA. The US GOVERNMENT will have the right of access to the full documentation for the [†] as agreed in the contract.

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: AVI will send an electronic and a paper copy of the approved [†] to the USG Program Office.

3.6.6.1 Ensure completion of [†] at CMO: The CMOs and manufacturers of some of the components of the final drug product configuration [†]. A copy of the CMO's Letter of Authorization permitting the FDA to access their confidential information in connection with the [†] will have been submitted in the [†]. AVI will endeavor to ensure that the CMO updates and maintains the conditions of the [†].

Period of Work: Approximately [†] day (e.g. [†]).

Deliverable: A copy of the Letter of Authorization for FDA to access the DMF information in connection with the review of the [†].

3.6.6.2 Submit Letter of Authorization for FDA review of [†] to US Government: The CMOs and manufacturers of some of the components of the final drug product configuration [†] will [†] that will be referenced by the name and address of the supplier and reference number in the [†]. A copy of the CMO's Letter of Authorization permitting the FDA to access their confidential information in connection with the [†] will have been submitted in the [†]. AVI will endeavor to ensure that the CMO updates and maintains the conditions of the [†].

Period of Work: Approximately [†] day (e.g. [†])

Deliverable: Deliver a copy of Letter of Authorization (to FDA) to USG.

3.6.6.3 Program management, operations and oversight: Develop timeline, manage vendors, anticipate and resolve problems, track project compliance, report project progress. As part of the normal course of executing project, regular team meetings will be held with each vendor and held internally. This team is responsible for the project plan. Project progress and any issues relative to the project plan will be documented and addressed with the Product Development Team on at least a monthly basis. Regular conference calls with the TMTI will be established to review progress and results.

Period of Work: Approximately [†] day (e.g. [†]).

† DESIGNATES PORTIONS OF THIS DOCUMENT THAT HAVE BEEN OMITTED PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT FILED SEPARATELY WITH THE COMMISSION.

Deliverable: Plan, monitor, and report overall delivery of milestones and budget.

3.6.7 Contract Program Management: AVI will track progress on each element in the contract, including all financial and reporting requirements; ensure compliance with contract and all government regulations. AVI will manage all subcontracts and ensure that their timelines are met, and the components contributed by each to the overall study are coordinated, on budget, and that they are compliant with all contract and Government regulations that are applicable.

Period of Work: Concurrent with all CLIN0008 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract management and financial oversight ensuring compliance.

3.6.7.1 Program Management: Track progress and manage issues as they arise.

Period of Work: Concurrent with all CLIN0008 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project management ensuring compliance.

3.6.7.2 Finance and [†]: Track financial work process and reporting.

Period of Work: Concurrent with all CLIN0008 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide project financial management ensuring compliance.

3.6.7.3 Contract and Subcontract Management: Manage our compliance with contract and USG regulations; manage subcontractors and relationship with them.

Period of Work: Concurrent with all CLIN0004 activities, a period of approximately [†] days (e.g. [†]).

Deliverable: Provide contract and subcontract management ensuring compliance.

3.6.7.4 EDMS and QA: The EDMS will have been fully implemented and routinely used to prepare, review and store documents for the [†], and regulatory and quality compliance documents. AVI will continue to store all documents in the validated EDMS and will make electronic document submissions to the FDA, as needed. AVI will train all pertinent staff on the EDMS, including Quality Assurance staff.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: EDMS system fully operational. QA audits of all vendors will have been performed and any follow up action items identified and tracked.

3.6.8 Drug Substance and Drug Product Ongoing Stability Studies: Continue manufacturing assessment of stability [†] prepared in CLIN0006.

Period of Work: Approximately [†] days (e.g. [†]).

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Deliverable: Continue assessment of stability study data (to include both drug substance and drug product).

3.6.8.1 Continue Drug Substance Stability Studies: Continue stability study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Continue assessment of drug substance stability data.

3.6.8.2 Continue Drug Product Stability Studies: Continue stability study.

Period of Work: Approximately [†] days (e.g. [†]).

Deliverable: Continue assessment of drug product stability data.

† DESIGNATES PORTIONS OF THIS DOCUMENT THAT HAVE BEEN OMITTED PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT FILED SEPARATELY WITH THE COMMISSION.

EXHIBIT 31.1

CERTIFICATION

I, Christopher Garabedian, certify that:

1. I have reviewed this Amendment No. 1 to Quarterly Report on Form 10-Q of AVI BioPharma, Inc., (the "Registrant"); and

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.

February 15, 2012

/s/ Christopher Garabedian
Christopher Garabedian
President and Chief Executive Officer
(Principal Executive and Financial Officer)

EXHIBIT 31.2

CERTIFICATION

I, Michael Jacobsen, certify that:

1. I have reviewed this Amendment No. 1 to Quarterly Report on Form 10-Q of AVI BioPharma, Inc., (the "Registrant"); and

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.

February 15, 2012

/s/ Michael Jacobsen
Michael Jacobsen,
Vice President, Finance
(Principal Accounting Officer)