

Non-Federal

## Subaward Agreement

Prime Awardee  
Institution/Organization ("PRIME RECIPIENT")

Name: Shuttle Pharmaceutical, LLC

Address: 1 Research Court, Suite 450  
Rockville, MD 20850

Prime Award No.

HHSN261201400013C

Sponsor

National Cancer Institute

Subawardee  
Institution/Organization ("SUBRECIPIENT")

Name: Rhode Island Hospital

Address: 593 Eddy Street  
Providence, RI 02903

Subaward No.

Subaward Period of Performance

Amount Funded this Action

Est. Total (if incrementally funded)

Phase I 10/27/14 - 6/18/15 Phase II 6/19/15 - 6/18/17

\$65,549

\$688,818

Project Title

Development of Radiation Modulators for Use During Radiotherapy

Reporting Requirements [Check here if applicable: ☒ See **Attachment 4**]

## Terms and Conditions

- 1) Prime Recipient hereby awards a cost reimbursable subaward, as described above, to Subrecipient. The statement of work and budget for this subaward are (check one):      as specified in Subrecipient's proposal dated           ; or   X   as shown in **Attachments 3 & 4**. In its performance of subaward work, Subrecipient shall be an independent entity and not an employee or agent of Prime Recipient.
- 2) Prime Recipient shall reimburse Subrecipient not more often than monthly for allowable costs. All invoices shall be submitted using Subrecipient's standard invoice, but at a minimum shall include current and cumulative costs (including cost sharing), subaward number, and certification as to truth and accuracy of invoice. *Invoices that do not reference Prime Recipient's subaward number shall be returned to Subrecipient.* Invoices and questions concerning invoice receipt or payments should be directed to the appropriate party's Financial Contact, as shown in **Attachment 2**.
- 3) A final statement of cumulative costs incurred, including cost sharing, marked "FINAL," must be submitted to Prime Recipient's Administrative Contact NOT LATER THAN sixty (60) days after subaward end date. The final statement of costs shall constitute Subrecipient's final financial report.
- 4) All payments shall be considered provisional and subject to adjustment within the total estimated cost in the event such adjustment is necessary as a result of an adverse audit finding against the Subrecipient.
- 5) Matters concerning the technical performance of this subaward should be directed to the appropriate party's Project Director, as shown in **Attachment 2**. Technical reports are required as shown above, "Reporting Requirements."
- 6) Matters concerning the request or negotiation of any changes in the terms, conditions, or amounts cited in this subaward agreement should be directed to the appropriate party's Administrative Contact, as shown in **Attachment 2**. Any such changes made to this subaward agreement require the written approval of each party's Authorized Official, as shown in Attachment 2.
- 7) Each party shall be responsible for its negligent acts or omissions and the negligent acts or omissions of its employees, officers or directors, to the extent allowed by law.
- 8) Either party may terminate this agreement with thirty days written notice to the appropriate party's Administrative Contact, as shown in **Attachment 2**. Prime Recipient shall pay Subrecipient for all allowable, noncancellable obligations in the event of termination.
- 9) No-cost extensions require the approval of the Prime Recipient. Any requests for a no-cost extension should be addressed to and received by the Administrative Contact, as shown in **Attachment 2**, not less than thirty days prior to the desired effective date of the requested change.
- 10) The Subaward is subject to the terms and conditions of the Prime Award and other special terms and conditions, as identified in **Attachment 1**.

By an Authorized Official of PRIME RECIPIENT:

By an Authorized Official of SUBRECIPIENT:

/s/ Anatoly Dritschilo10/22/2014□10/28/2014

Anatoly Dritschilo, MD - CEO

Date

Date

Lifespan 3/15/10

**Attachment 2**  
**Subaward Agreement**

**Administrative Contact**      Prime Recipient Contacts

Name: Peter D. Dritschilo  
President & CFO

Address: Shuttle Pharmaceuticals, LLC  
One Research Court, Suite 450  
Rockville, MD 20850-6252

Telephone: 240-271-0642  
Fax: 301-519-8081  
Email: hoy92@aol.com

**Principal Investigator**

Name: Theodore Phillips, MD

Address: Shuttle Pharmaceuticals, LLC  
One Research Court, Suite 450  
Rockville, MD 20850-6252

Telephone: 240-403-4212  
Fax: 301-519-8081  
Email: farfa12@aol.com

**Financial Contact**

Name: Peter D. Dritschilo President & CFO  
President & CFO

Address: Shuttle Pharmaceuticals, LLC  
One Research Court, Suite 450  
Rockville, MD 20850-6252

Telephone: 240-271-0642  
Fax: 301-519-8081  
Email: hoy92@aol.com

**Authorized Official**

Name: Anatoly Dritschilo, MD CEO

Address: Shuttle Pharmaceuticals, LLC  
One Research Court, Suite 450  
Rockville, MD 20850-6252

Telephone: 202-444-4068  
Fax: 301-519-8081  
Email: dritscha@georgetown.edu

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**Administrative Contact**      Subrecipient Contacts

Name: Kim-Marie Lawrence

Address: Office of Research Administration  
1 Hoppin Street, Suite 1,300  
Providence, RI 02903-4141

Telephone: 401.444.8554  
Fax: 401.444.4061  
Email: klawrence@lifespan.org

**Project Director**

Name: Timothy Kinsella, MD  
“Essential to the project.”

Address: Rhode Island Hospital  
593 Eddy Street, APC 1  
Providence, RI 02903

Telephone: 401.444.6203  
Fax: 401.444.5335  
Email: tkinsella@lifespan.org

**Financial Contact**

Name: Donald Hook  
Manager, Research Finance

Address: Rhode Island Hospital  
1 Hoppin Street, Suite 1.300  
Providence, RI 02903-4141

Telephone: 401-444-5112  
Fax: 401-444-4061  
Email: dhook@lifespan.org

**Authorized Official**

Name: Joan M. Silva

Address: Administrative Manager  
Rhode Island Hospital  
Office of Research Administration  
1 Hoppin Street, Suite 1.300  
Providence, RI 02903-4141

Telephone: 401.444.4006  
Fax: 401.444.4061  
Email: jsilva@lifespan.org

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Proposed Budget - Attachment 3

701.xxxx

IPdR (BrUOG 265)

Tim Kinsella, MD

Tim Kinsella, MD			Start End	10/22/14 6/18/15		6/19/15 6/18/16			6/19/16 6/18/17		
Personnel	Salary	Cal Mos.	Effort	Yr 1	Cal Mos.	Effort	Yr 2	Cal Mos.	Effort	Yr 3	TOTAL
Tim Kinsella, MD	\$ 181,500	1.45	12.1%	\$ 16,448	2.76	23%	\$ 41,745	2.76	23%	\$ 41,557	\$ 99,750
Howard Safran, MD	\$ 181,500	0.47	3.9%	\$ 5,332	1.08	9%	\$ 16,335	1.08	9%	\$ 16,335	\$ 38,002
Andrea Monckeberg,	\$ 125,000		0.0%	\$ 0	0.36	3%	\$ 3,825	0.36	3%	\$ 3,902	\$ 7,727
Mark LeGolván, MD	\$ 181,500			\$ 0	0.00	0%		0.23	2%	\$ 3,479	\$ 3,479
TBN, CRA	\$53,500	1.70	14.2%	\$ 5,684	1.70	14.2%	\$ 5,798	1.70	14.2%	\$ 5,914	\$17,396
TBN, Res Nurse	\$ 87,210		0.0%	\$ 0	6.60	55%	\$ 47,966	6.60	55%	\$ 48,925	\$ 96,890
Total Salaries				\$ 27,464			\$ 115,669			\$ 120,111	\$ 263,244
Fringe:				31.9%							
Tim Kinsella, MD				\$ 5,247			\$ 13,317			\$ 13,257	\$ 31,820
Howard Safran, MD				\$ 1,701			\$ 5,211			\$ 5,211	\$ 12,122
Andrea Monckeberg,				\$ 0			\$ 1,220			\$ 1,245	\$ 2,465
Mark LeGolván, MD				\$ 0			\$ 0			\$ 1,110	\$ 1,110
TBN, CRA				\$ 1,813			\$ 1,850			\$ 1,887	\$ 5,549
TBN, Res Nurse				\$ 0			\$ 15,301			\$ 15,607	\$ 30,908
Total Fringe Benefits				\$ 8,761			\$ 36,898			\$ 38,315	\$ 83,975
Total Sal + Fringe				\$ 36,226			\$ 152,567			\$ 158,427	\$ 347,219
Equipment				\$ 0			\$ 0			\$ 0	\$ 0
Supplies											
Animal				\$ 0			\$ 0			\$ 0	\$ 0
Lab Supplies				\$ 0			\$ 0			\$ 0	\$ 0
Total Supplies				\$ 0			\$ 0			\$ 0	\$ 0
Travel				\$ 0			\$ 0			\$ 0	\$ 0
Other											
Publications				\$ 0			\$ 0			\$ 0	\$ 0
BrUOG				\$ 5,000			\$ 37,500			\$ 37,500	\$ 80,000
Biopsy costs/ processing				\$ 0			\$ 0			\$ 6,000	\$ 6,000
Total Other				\$ 5,000			\$ 37,500			\$ 43,500	\$ 86,000
Total Direct				\$ 41,226			\$ 190,067			\$ 201,927	\$ 433,219
Less: Equipment				\$ 0			\$ 0			\$ 0	\$ 0
MTDC Indirect Base x Indirect Rate (59% as of 10/01/11)				\$41,226 59%			\$190,067 59%			\$201,927 59%	\$433,219 59%
Indirect Costs				\$ 24,323			\$ 112,139			\$ 119,137	\$ 255,599
Total Costs				\$ 65,549			\$ 302,206			\$ 321,063	\$ 688,818

**ATTACHMENT 4  
SUBAWARD AGREEMENT**

This attachment provides a (1) a statement of flowdown clauses from the prime contract # HHSN261201400013C, (2) precedence of the prime contract (3) statement of work and (4) reporting requirements for Phase I and Phase II.

**Flowdown Clauses**

Line 10 of the subaward agreement states "The Subaward is subject to the terms and conditions of the Prime Award and other special terms and conditions, as identified in Attachment 1." The Items are in sections H and I of the contract # HHSN261201400013, included in Attachment 1.

**Order of Precedence**

This Contract, together with the enumerated Attachments (1-4) hereto (all of which are incorporated herein by this reference) shall comprise this Contract and shall together be referred to as the "Sub-contract Documents." In the event of any inconsistencies between this Contract and the Prime Contract HHSN2612014800013C, as included in Attachment 1, the prime contract will have precedence in the interpretation or resolution of such conflict.

**Statement of Work - Subcontract**

**I. Background Information and Objectives**

For NIH review of the Lifespan/RIH subcontract and the subcontract statement of work the following summary is provided. The subcontractor will work with the PI and the prime contractor to accomplish the following tasks. The full SOW is included in the signed contract # HHSN261201400013C.

**PHASE I SBIR**

**A. Technical Objectives**

**Objective 1. Activate the IPdR IND for the Phase I and PK clinical trial.**

**Task 1.1.** File administrative documents to initially cross-file (IND 70,333) and obtain an IND for the IPdR and RT clinical trial.

**Milestone 1.1.** An IPdR IND.

**Task 1.2.** Negotiate with CTEP to transfer sufficient clinical product IPdR for performance of the clinical trial.

**Milestone 1.2.** Clinical product (encapsulated) IPdR, will be made available for the proposed Phase I and PK clinical trial at Lifespan/RIH.

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**Objective 2. Obtain approvals for the Phase I and PK clinical protocol. Develop efficacy protocols satisfying FDA “Orphan Drug” status.**

- Task 2.1.** Submit a Letter of Intent (LOI) to NCI CTEP for the Phase I and PK clinical studies of IPdR.  
**Milestone 2.1.** LOI approval.  
**Task 2.2.** Submit to the IRB the Phase I and PK study protocol.  
**Milestone 2.2.** IRB approval of the Phase I study for IPdR + RT.  
**Task 2.3.** Consult with the FDA regarding "Orphan Drug" status for IPdR  
**Milestone 2.3.** FDA guidance on "Orphan Drug" status for IPdR for rectal cancer.

**Objective 3. Establish the in-house (Shuttle Pharmaceuticals, LLC Laboratories) biomarker assays.**

- Task 3.1** will be performed at NIH and Shuttle Pharmaceuticals  
**Task 3.2.** Prepare a written report of Phase I SBIR achievements to NIH.  
**Milestone 3.2.** NIH accepts the report and exercises the option for Phase II.

**Gantt Chart 1: Phase I. Milestones, Deliverables Timeline & Work Distribution. between Shuttle Pharmaceuticals, LLC (SP) and Lifespan/Rhode Island Hospital (L/RIH).**

Site	Milestones and Deliverables	Months								
		1	2	3	4	5	6	7	8	9
SP, L/RIH	<i>Objective 1. Task 1.1.</i> <b>Milestone 1.1.</b> Activation of the IPdR IND									
SP	<i>Objective 1. Task 1.2.</i> <b>Milestone 1.2.</b> IPdR clinical product for use in the Phase I clinical trial									
SP	<i>Objective 1. Task 1.3.</i> <b>Milestone 1.3.</b> Capsules of IPdR for Phase I.									
SP, L/RIH	<i>Objective 2. Task 2.1.</i> <b>Milestone 2.1.</b> CTEP approval of the Phase I and PK LOI.									
SP, L/RIH	<i>Objective 2. Task 2.2.</i> <b>Milestone 5.</b> IRB approval of the Phase I clinical trial.									
SP	<i>Objective 2. Task 2.3.</i> <b>Milestone 6.</b> FDA advice regarding "Orphan Drug" status for IPdR in rectal cancer treatment.									
SP	<i>Objective 3. Task 3.1.</i> <b>Milestone 3.1.</b> The GLP %IUdR-DNA cellular incorporation assays established in SP laboratories.									
SP	<i>Objective 3. Task 3.2.</i> <b>Milestone 3.2.</b> NIH approves final report and exercises the Phase II option.									

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## PHASE II SBIR

### A. Technical Objectives

#### **Objective 1: Perform the Phase I and PK clinical trial of IPdR-mediated radiosensitization.**

**Task 1.1.** Perform the Phase I clinical trial.

**Milestone 1.1.** Collect clinical data.

**Milestone 1.3.** Collect and transfer clinical samples to SP Laboratories for analysis.

#### **Objective 2: Perform PK analyses to determine optimal dosing schedule.**

**Task 2.1.** Determine pharmacokinetics (PK) and %IUdR-DNA for biomarker analysis.

**Milestone 2.1.** Clinical specimens are obtained and analyzed for PK & % IUdR-DNA.

**Milestone 2.2.** PK analyses results.

**Milestone 2.3.** %IUdR-DNA incorporation results and clinical correlation.

#### **Objective 3: Use Phase I and PK results to design the Phase IB/II clinical trial.**

**Task 3.1.** Analyze the PK data to determine optimal IPdR dosing.

**Milestone 3.1.** Optimum dosing schedule of IPdR is established.

**Task 3.2.** Design and write the Phase IB/II protocol for efficacy determination.

**Milestone 3.2.** Phase IB/II clinical protocol for IPdR and RT in rectal cancer.

#### **Objective 4: Advance the business development and commercialization plan.**

**Task 4.1.** Use Phase I clinical trial results to raise capital for efficacy clinical trials.

**Milestone 4.1.** Written business development and commercialization.

**Task 4.2.** Prepare a final written report for the Government Project Officer.

**Milestone 4.1.** Written final progress report is accepted.

#### **Gantt Chart 2: Phase II Milestones, Deliverables and Work Distribution.**

Site	Milestones and Deliverables	Delivery Schedule (months)											
		2	4	6	8	10	12	14	16	18	20	22	24
L/RIH	<u>Objective 1, Task 1.1</u> <b>Milestone 1.1.</b> Initiation and performance of the Phase I and PK clinical trial of IUdR with RT. <b>Milestone 1.2.</b> Safety and MTD parameters for IPdR with RT. <b>Milestone 1.3.</b> Collect and transfer clinical samples to SP Labs.												
L/RIH	<u>Objective 2, Task 2.1</u> <b>Milestone 2.1.</b> Obtain clinical specimens for PK & %IUdR-DNA <b>Milestone 2.2.</b> PK analyses												
SP	<b>Milestone 2.3.</b> %IUdR-DNA incorporation is determined and correlated with clinical observations.												
SP	<u>Objective 3: Task 3.1</u> <b>Milestone 3.1.</b> Dosing schedule of IPdR is established, based on PK												
SP	<u>Objective 3: Task 3.2</u> <b>Milestone 3.2.</b> Written Phase IB/II clinical protocol												
SP	<u>Objective 4: Task 4.1</u> <b>Milestone 4.1</b> Written business and commercialization plan.												
SP,	Objective 4: Task 4.2.												
L/RIH	<b>Milestone 4.2.</b> Final report submitted to NIH.												

Shuttle Pharmaceuticals, LLC (SP); Lifespan/Rhode Island Hospital (L/RIH)

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## Reporting Requirements

### Phase I

1.	Kick-off presentation 10/16/14	
2.	Phase I, two quarterly reports	12/19/14 and 3/19/15
3.	Draft Updated Commercialization Plan	5/18/15
4.	Draft Final Report and Draft Summary of Salient Results	6/18/15
5.	Final Commercialization Plan	6/18/15
6.	Final Report	6/18/15
7.	Final Presentation	6/18/15

Phase II contract activities and reporting will be contingent on the Government's decision to exercise the option per Article B.# of the contract # HHSN261201400013C.

### Phase II

1.	Option exercised	(approximately) 6/19/15
2.	Phase II, quarterly reports exercises	every 90 days after option
3.	Draft Final Report for Phase II and Summary of Salient Clinical Trial Results	5/19/17
4.	Draft Phase II Final Report	6/19/17
5.	Phase II Final Report and Presentation	6/19/17
6.	Summary of Salient Clinical Trial Results	6/19/17

### Additional Reporting and Certifications

7.	Annual technical progress report for Clinical Research Study Populations	6/19/17
8.	Protection of Human Subjects	6/19/15
9.	Annual Utilization	6/19/16
10.	Final Invention Statement and Disclosure	6/19/17
11.	Annual Report	6/19/16
12.	Conformance Certification	6/19/15
13.	Financial Conflict of Interest	as it arises
14.	Life Cycle Phase I	6/18/15
15.	Life Cycle Phase II Report 1	6/18/16
16.	Life Cycle Phase II Report 2	6/18/17

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