18-04338-E

foiapa

From: Mark Edwards <medwards@biosciadvisors.com>
Sent: Friday, May 11, 2018 6:48 PM
To: foiapa
Subject: FOIA Request

I would like to request access to Exhibit 10.5 to the 3/31/15 10-Q, filed by Regulus Therapeutics, Inc. on 5/8/2015. Confidential treatment was sought as to certain portions when initially filed with the Commission.

In the event that confidential treatment has not expired or has been extended, I further request that you send me the expiration date(s) from the relevant CT order(s) so I will know when I should resubmit my request.

I authorize up to $61 in search and retrieval fees. Please send the exhibit(s) by PDF if possible.

Sincerely,

Mark

Mark G Edwards
Managing Director
Bioscience Advisors
2855 Mitchell Dr., Suite 103
Walnut Creek, CA 94598
medwards@biosciadvisors.com
925 954-1397

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

May 31, 2018

Mr. Mark G. Edwards
Bioscience Advisors
2855 Mitchell Dr., Suite 103
Walnut Creek, CA 94598

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-04338-E

Dear Mr. Edwards:

This letter is in response to your request, dated May 11, 2018 and received in this office on May 14, 2018, for access to Exhibit 10.5 to the Form 10-Q filed by Regulus Therapeutics, Inc. on May 8, 2015.

The search for responsive records has resulted in the retrieval of 6 pages of records that may be responsive to your request. They are being provided to you with this letter.

As shown on the enclosed invoice, the processing fee is $30.50 in accordance with our fee schedule. You may use our Online Payment option to pay by debit or credit card. If paying by mail, checks or money orders should be made payable to the SEC and a copy of the invoice should be mailed to our payment address: Enterprise Services Center, HQ Bldg., Room 181, AMZ-341, 6500 South MacArthur Boulevard, Oklahoma City, OK 73169. Please refer to the following link for detailed instructions on how to remit payments. http://www.sec.gov/about/offices/ofm.htm

If you have any questions, please contact me at taylorf@sec.gov or (202) 551-8349. You may also contact me at foiapa@sec.gov or (202) 551-7900. You also have the right to seek assistance from Dave Henshall as a FOIA Public Liaison or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

Felecia Taylor

Felecia Taylor
FOIA Lead Research Specialist

Enclosures

January 28, 2015

AstraZeneca AB
S-431 83,
Mölndal, Sweden
Attention: Marcus Schindler

Re: Payment and Responsibilities for [IND-enabling] Studies and Manufacture of Phase 1 Clinical miR-103/107 Product

Dear Marcus:

This letter will confirm our discussions and agreement regarding the respective responsibilities and payment obligations of Regulus and AstraZeneca concerning [IND-enabling] studies and Manufacturing of clinical Product for Phase 1 in the miR103/107 program.

Listed in Exhibit A, attached hereto, are the [Pre-IND] studies and the API Manufacturing activities necessary for such studies related to the miR-103/107 program and their anticipated cost. AstraZeneca and Regulus agree the studies and API Manufacturing activities will be managed by Regulus.

Regulus and AstraZeneca will each pay fifty percent (50%) of the total costs for activities set forth on Exhibit A. Any change in the scope of the activities set forth on Exhibit A shall also be borne on a fifty-fifty basis. It is anticipated that changes to the activities set forth in Exhibit A may be requested from time to time. Any change which will result in a [10% or greater] increase in the cost of any activity will only be made upon the written consent of each party's chairperson for the JSC, however all changes which result in an increase in cost will be agreed within the Joint Project Team (JPT).

In order to fund fifty percent of the activities in Exhibit A, within thirty (30) Business days of the above date and receipt of an invoice, AstraZeneca shall advance fifty percent of the costs which are anticipated to be incurred during the current calendar quarter. Regulus shall make timely payments for the studies and API Manufacturing activities as they become due utilizing the AstraZeneca advanced funds, on a fifty-fifty basis. At least forty-five (45) Business Days before the end of each subsequent calendar quarter, and until all agreed upon activities have been completed, Regulus shall provide an estimate of the amounts expected to be paid in the following calendar quarter. AstraZeneca shall pay within 45 business days upon receipt of an invoice for such estimates. In addition, at the end of each calendar quarter, Regulus shall provide to AstraZeneca an accounting of the payments made for the activities, along with supporting documentation. Upon completion of the activities set forth in Exhibit A, and settlement of all related due and payable invoices, Regulus shall provide a final reconciliation of all

amounts paid for the activities. If a balance is due to Regulus, AstraZeneca shall pay such balance within forty-five (45) Business Days of receipt of the invoice for the final reconciliation. Otherwise, Regulus shall refund any funds remaining to AstraZeneca with the final reconciliation.

Set forth in Exhibit B are the agreed upon Manufacturing activities and cost thereof necessary to support the first Phase 1 study Product. The parties agree that Regulus will manage these activities with the manufacturer with input from the JSC. The parties also agree that Regulus will be reimbursed as set forth in Section 4.1 of the Collaboration and License Agreement. If, however, the activities listed on Exhibit B are delayed or cancelled and such delay or cancellation results in charges to Regulus, the Parties agree they will each bear fifty percent of the charges attributable to the cancellation or delay.

In order to fund the activities set forth in Exhibit B, AstraZeneca shall pre-fund [100%] of the cost of the anticipated Product activities for each calendar quarter as set forth above and the parties shall follow the same reimbursement and documentation structure.

Any capitalized terms herein shall be governed by the terms of the Collaboration and License Agreement.

Please confirm your agreement with the above terms by returning a signed copy of this letter to my attention.

Sincerely,

/s/ Neil W. Gibson, Ph.D.

Neil W. Gibson, Ph.D.
Chief Scientific Officer

Signed and Agreed on behalf of AstraZeneca AB:

/s/ Jan-Olof Jacke

Name: Jan-Olof Jacke (on behalf of Marcus Schindler)

Title: President

Date: 1/30/2015

EXHIBIT A

version 4.3

Project: RG-125 (miR-103, RG3470)
Phase: IND-Enabling Toxicology

Proposed Service Provider	Activity or Study	Cost Estimates: Regulus Option A (Single Dose GLP Tox)	Cost Estimates: JSC Agreed Option B (for 6 Week GLP Tox)	NOTES	Timing	Payment Terms	50% estimated cost per quarter (based on payment terms)				
							1Q2015	2Q2015	3Q2015	4Q2015	2016
IND-Enabling Tox Studies and ADME											
SNBL	Single-Dose Range Finding Toxicity and Toxicokinetic Study in Mice (GLP)	$118,900		SNBL est. 17754 (minus BA), includes DFA		n/a					
SNBL	Single-Dose Range Finding Toxicity and Toxicokinetic Study in Cynomolgus Monkeys (GLP)	$242,000		SNBL est. 17758 (minus BA), includes DFA		n/a					
SNBL	CV/Resp Safety Pharm in Concious Telemeterized Cynos (GLP)	$69,920		SNBL est. 16456, includes DFA		n/a					
SNBL	6 Week Tox in Mice w/8 Week Recovery (GLP)		$307,300	SNBL est. 17709, includes DFA	Start last wk Jan	40% at study initiation (end Jan 2015), 50% end in-life (April), 10% Report (July)	$61,460	$76,825	$15,365		
SNBL	6 Week Tox in Cyno w/8 week recovery, including CV/Resp Pharmacology (GLP)		$513,300	SNBL est. 17753, includes DFA	Start 2nd wk April	40% at study initiation (April 2015), 50% end in-life (July), 10% Report (Oct)		$102,660	$128,325	$25,665	
WIL Res	AMES Test (GLP)- DFA at SNBL ($1700)	$10,000	$10,000	Est. from previous project	Q2			$5,000			
WIL Res	Chrom Ab Tests (GLP)- DFA at SNBL ($1700)	$35,000	$35,000	Est. from previous project	Q2			$17,500			
	CYP induction and inhibition			TBD, possibly perform by AZ							
SNBL	DFA method development/validation for all GLP tox studies	$17,100	$17,100	Needed to support GLP studies	Start early Jan		$8,550				
Avecia	Dose formulation stability analysis for mouse GLP tox	$21,250	$21,250	Needed to support GLP studies	Start early Jan		$10,625				
Avecia	Dose formulation stability analysis for NHP GLP tox	$21,250	$21,250	Needed to support GLP studies	Start early March			$10,625			
	Total	$535,420	$935,200				$80,635	$212,610	$143,690	$25,665	$0
Bio-Analytical (estimates based on past experience; more accurate estimates pending decision on analysis method, study design (sample #), and number of analytes to be quantitated)											
Tandem	MD/MV for mouse plasma	$38,000	$38,000	Need for both SD and Repeat dose	Q1	MD cost is billed by # of days quoted in the contract; MD/MV is billed as one payment; for any cancellation of MD/MV, Tandem would charge based on amount of work completed up to the time of cancellation.	$19,000				
Tandem	MD/MQ mouse urine		$17,000	Need for both SD and Repeat dose	Q1		$8,500				
Tandem	MD/MQ mouse tissues	$22,500	$22,500	Need for both SD and Repeat dose	Q1		$11,250				
Tandem	MD mouse metabolite profiling	$5,000	$5,000	Need for both SD and Repeat dose	Q1		$2,500				
Tandem	MD/MV cyno plasma	$58,000	$58,000	Need for both SD and Repeat dose	Q1		$29,000				
Tandem	MD/MQ cyno urine		$17,000	Need for both SD and Repeat dose	Q1		$8,500				
Tandem	MD/MQ cyno tissues	$15,000	$15,000	Need for both SD and Repeat dose	Q1		$7,500				
Tandem	MD cyno metabolite profiling	$5,000	$5,000	Need for both SD and Repeat dose	Q1		$2,500				
Tandem	Analysis mouse plasma for single dose GLP tox study approx 114 samples (+10% ISR)	$12,500		assume $100/sample for 3 analytes	Q2						
Tandem	Analysis mouse tissues for single dose GLP tox study approx 372 samples (+10% ISR)	$47,040		assume $115/sample for 3 analytes	Q2						
Tandem	Analysis cyno plasma for singles dose GLP tox study approx 300 samples (+10% ISR)	$33,000		assume $100/sample for 3 analytes	Q2						
Tandem	Analysis cyno tissues for single dose GLP tox study approx 120 samples (+10% ISR)	$15,180		assume $115/sample for 3 analytes	Q2						
Tandem	Analysis mouse plasma for 6 wk GLP tox study approx 150 samples (+10% ISR)		$16,500	assume $100/sample for 3 analytes	Q2			$8,250			
Tandem	Analysis mouse tissue for 6wk GLP tox study approx 525 samples (no ISR for non-GLP analysis)		$57,750	assume $115/sample for 3 analytes	Q2			$28,880			
Tandem	Analysis mouse urine for single 6 wk GLP tox study approx 20 samples (no ISR for non-GLP analysis)		$2,000	assume $100/sample for 3 analytes		Only charged for actual number of samples analyzed		$1,000			
Tandem	Analysis mouse metab profiling (plasma & tissues, 6 wk tox) approx 400 samples (+10% ISR)		$60,000	This may be performed at Regulus (FTE cost to be determined)	Q2			$30,000			
Tandem	Analysis cyno plasma for 6wk GLP tox study approx 770 samples (+10% ISR)		$84,700	assume $100/sample for 3 analytes	Q2			$42,350			
Tandem	Analysis cyno tissue for 6wk GLP tox study approx 110 samples (no ISR for non-GLP analysis)		$13,900	assume $115/sample for 3 analytes	Q2			$6,950			
Tandem	Analysis cyno urine for 6wk GLP tox study approx 12 samples (no ISR for non-GLP analysis)		$1,300	assume $100/sample for 3 analytes	Q2			$650			
Tandem	Analysis cyno metab profiling (plasma, urine & tissues, 6 wk tox study) approx 400 samples (+10% ISR)		$60,000	This may be performed at Regulus (FTE cost to be determined)	Q2			$30,000			
PNA Bio	Probes for BA work	$15,000	$15,000	ESTIMATE 1 probe, 2 orders	Q1		$7,500				
	Total	$266,720	$488,650				$96,250	$148,080	$0	$0	$0
Drug Substance Manufacture and Analytical											
Avecia	Forced Degradation Study	$60,000	$60,000	Activities supporting both GLP studies and CMC for IND and Phase I Costs to be split 50/50 (reflected in Quaterly costs)	See Timing and Decisions Tab		$30,000				
Avecia	MD/MQ of IP-RP-HPLC-UV-MS and IEX-HPLC methods	$140,000	$140,000				$35,000	$35,000			
Avecia	MD/MQ of API Sequencing	$20,000	$20,000					$10,000			
Avecia	MD/MQ of Tm method	$15,000	$15,000					$7,500			
Avecia	Synthesis and release testing of Complement Strand	$10,000	$10,000				$5,000				
Avecia	Preparation and certification/characterization of primary API reference standard	$75,000	$75,000				$37,500				
Avecia	Preparation and Qualification of Liquid Reference Standards and determination of molar extinction coefficient	$50,000	$50,000					$25,000			
Avecia	non-GMP DS Stability (supportive, short term)	$40,000	$40,000				$10,000	$10,000			
Avecia	non-GMP DS Stability (longer term)	$55,000	$55,000				$10,000	$4,000	$4,000	$4,000	$5,500
Avecia	Incoming goods test for non-GMP DS Manufacturing campaigns	$8,500	$8,500				$4,250				
Avecia	Non GMP API Manufacture in GMP facility - Total of 0.15 kg DS (Based on UV purity correction of 88%, moisture 15%) including release testing	$199,000	$199,000	First 37 mmol batch for GLP studies	Starting Jan 19, release end March	Contract signed, need decision from AZ by Jan 7 (for repurposing)	$99,500				
Avecia	Non GMP API Manufacture in GMP facility - Total of 0.15 kg DS (Based on UV purity correction of 88%, moisture 15%) including release testing		$199,000	Second 37 mmol batch for GLP studies	Starting Jan 19 pending decision, release end March	Contract signed, need decision from AZ by Jan 7 (for repurposing)	$99,500				
ST Pharm	cEt-A for 37 mmol batch (first batch) 610 grams	$16,165	$16,165	$26.50/g	All amidites and GalNAc have been ordered for stock re-supply		$8,083				
ST Pharm	cEt-A for 37 mmol batch (second batch) 610 grams		$16,165				$8,083				
ST Pharm	cEt-C for 37 mmol batch (first batch) 550 grams	$15,015	$15,015	$27.30/g			$7,508				
ST Pharm	cEt-C for 37 mmol batch (second batch) 550 grams		$15,015				$7,508				
ST Pharm	cEt-G for 37 mmol batch (first batch) 390 grams	$11,388	$11,388	$29.20/g			$5,694				
ST Pharm	cEt-G for 37 mmol batch (second batch) 390 grams		$11,388				$5,694				
ST Pharm	cEt-U for 37 mmol batch (first batch) 350 grams	$8,750	$8,750	$25.00/g			$4,375				
ST Pharm	cEt-U for 37 mmol batch (second batch) 350 grams		$8,750				$4,375				
Davos/Anthem	GalNAc succinate for 37 mmol batch (first batch) 135 grams	$15,525	$15,525	$115/g			$7,763				
Davos/Anthem	GalNAc succinate for 37 mmol batch (first batch) 135 grams		$15,525				$7,763				
Kinovate	GalNAc solid support for 37 mmol batch (first batch) 270 grams	$6,480	$6,480	$24/g			$3,240				
Kinovate	GalNAc solid support for 37 mmol batch (first batch) 270 grams		$6,480				$3,240				
	Total	$745,823	$1,018,146				$404,073	$91,500	$4,000	$4,000	$5,500
Total		**$1,547,463**	**$2,431,996**				**$580,958**	**$452,190**	**$147,690**	**$29,665**	**$5,500**
	Estimate of 50% Cost of Option B to be invoiced to AZ on quarterly basis		**$1,215,998**								

Costs in red predicted to be incurred prior to March 31

***Confidential Treatment Requested

EXHIBIT B

Project: RG-125 (miR-103, RG3470)

version 4.3 **Phase: Phase I Drug Manufacturing**

Proposed Service Provider	Activity	Cost Estimates	NOTES	Timing and Payment Terms	Estimated cost by quarter (based on payment terms)				
					1Q2015	2Q2015	3Q2015	4Q2015	2016+
Analytical									
Avecia	Forced Degradation Study		These activities and costs are accounted for in the IND-Enabling Study (Exhibit A) budget	See Timing and Decisions Tab					
Avecia	MD/MQ of IP-RP-HPLC-UV-MS and IEX-HPLC methods								
Avecia	MD/MQ of API Sequencing								
Avecia	MD/MQ of Tm method								
Avecia	Synthesis and release testing of Complement Strand								
Avecia	Preparation and certification/characterizatioin of primary API reference standard								
Avecia	Preparation and Qualification of Liquid Reference Standards and determination of molar extinction coefficient								
Avecia	non-GMP DS Stability (supportive, short term)								
Avecia	non-GMP DS Stability (longer term)								
Avecia	Incoming goods test for non-GMP DS Manufacturing campaigns								
Avecia	ICH Derived DS Stability Study (GMP clinical batch)	$75,000	GMP Clinical only (invoicing into 2017)				$20,000	$10,000	$45,000
Avecia	Incoming goods test for GMP DS Manufacturing campaigns	$8,500	GMP Clinical only			$8,500			
Avecia	Analytical Compendial Qualification (Bioburden, Endotoxin, Particulate Matter, Sterility, Osmo, pH)	$48,000	Needed to establish DP CMO fill/finish capabilities for GMP vials			$30,000	$18,000		
Avecia	Analytical Methods Transfer (IP-RP-HPLC-UV-MS) for DP mfr	$10,000				$10,000			
Avecia	Filled drug product in process UV method qualification	$15,000				$15,000			
Avecia	Identy testing of incoming Drug Substance for GMP DP production	$3,000	DP mfr preparation activity				$3,000		
Avecia	In-process testing of Bulk Drug Product (Bioburden , pH, UV, Osmo) - per lot	$2,000	DP mfr activity				$2,000		
Avecia	GMP Lot Release Testing of Final Filled Product (sterility, endotoxin, particulate matter, osmo, appearance, pH, UV, viscosity) per lot	$27,000	DP GMP vial release				$27,000		
Avecia	GMP Stability testing of Fill/Finish Drug Product	$125,000	Proposed DP vial stability study; invoicing into 2017				$25,000	$25,000	$75,000
Regulus	Regulus internal support (data analysis, QC, QA, PM); 1.15 FTE	$437,000			$109,250	$109,250	$109,250	$109,250	
	Total	$750,500			$109,250	$172,750	$204,250	$144,250	$120,900
Raw materials									
ST Pharm	cEt-A for 300 mmol batch, 3810 grams + 100% overage in case of batch failure (7620 grams)	$201,930	$26.50/g	Amidites and GalNAc have been ordered for stock Invoice for AZ in same quarter when batch is produced		$201,930			
ST Pharm	cEt-C for 300 mmol batch, 3440 grams + 100% overage in case of batch failure (6880 grams)	$187,825	$27.30/g			$187,825			
ST Pharm	cEt-G for 300 mmol batch, 2440 grams + 100% overage in case of batch failure (4880 grams)	$142,496	$29.20/g			$142,496			
ST Pharm	cEt-U for 300 mmol batch, 2190 grams + 100% overage in case of batch failure (4380 grams)	$109,500	$25.00/g			$109,500			
Davos/Anthem	GalNAc succinate for 300 mmol batch (first batch) 850 grams + 100% overage in case of batch failure (1700 grams)	$195,500	$115/g			$195,500			
Kinovate	GalNAc solid support for 300 mmol batch (first batch) 1700 grams + 100% overage in case of batch failure (3400 grams)	$81,600	$24/g			$81,600			
	Total	$918,851			$0	$918,851	$0	$0	$0
Drug Substance Manufacture									
Avecia	POC study for scale-up to 1 kg GMP API Manufacture	$70,000	Estimate		$70,000				
Avecia	GMP API Manufacture in GMP facility - Total of 0.7 kg DS (Based on UV purity correction of 88%, moisture 15%) including release testing	$1,217,000	300-310 mmol batch for clinical studies	FOR 13 APR MFR SLOT: 1) To hold slot at Avecia, contract must be signed by **Jan 31, 2015** 2) GMP batch release = mid-June (can be expedited to late May with extra fees) 3) **Invoice timing:** - 120 days prior to start date (Feb), 15% ($182.5K) - 60 days prior to start date (Feb), 15% ($182.5K) - at start (Apr), 20% ($243.4K) - at freeze-dry start (Apr), 20% ($243.4K) - Data summary issue (Jun), 30% ($365K) 4) **Cancellation terms:** - >90d from start (after contract approval), 5% + Avecia-supplied raw material ($61K+) - 60-90d (prior to 12 Feb), 30% ($365K) - 30-60d (between 12 Feb and 14 March), 60% ($730K)	$365,100	$486,800	$365,100		
Regulus	Regulus internal support (data analysis, QC, QA, PM); 0.55 FTE	$209,000			$52,250	$52,250	$52,250	$52,250	
	Total	$1,496,000			$487,350	$539,050	$417,350	$52,250	$0
Drug Product Manufacture									
Althea or Pyramid	GMP Fill/Finish Manufacture (~1 kg DS)	$300,000		Tentative DP mfg start Jun/July; slot cannot be booked without signed contract for Pyramid, if contract is cancelled per MSA, from date of planned mfg: > 6 wks = no charge; 4-6 wks = 25%; 3-4 wks = 50%; 2-3 wks = 75%; < 2 wks = 100%.			$150,000	$150,000	
Regulus	Regulus internal support (data analysis, QC, QA, PM); 0.35 FTE	$133,000			$33,250	$33,250	$33,250	$33,250	
	Total	$433,000			$33,250	$33,250	$183,250	$183,250	$0
Projected Total AZ Cost for Phase I Drug Supply to be invoiced quarterly		**$3,598,351**		**Total quarterly budget**	**$629,850**	**$1,663,901**	**$804,850**	**$379,750**	**$120,000**
				estimated cancellation fees (Avecia Mfg)- AZ pays 50% if occurs	$365,000 if cancel prior to 13Feb $730,000 if cancel between 13Feb and 14March				