From the desk of:

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APOTEX INC.
CANADA'S PHARMACEUTICAL COMPANY

Cecelia Parise, Regulatory Policy Advisor
Office of Generic Drugs

c/o Dockets Management Branch
Room 1061, Mail Stop HFA-305
5630 Fishers Lane
Rockville, MD 20852
(fax) 301-827-6870

Re: Ramipril Capsules and 180-day generic drug exclusivity
FDA Docket No. 2007N-0382

And

Petition for Stay of Action (PSA)

Dear Ms. Parise:

In further response to the above docket regarding generic ramipril capsules, we draw your attention to subsequent events that call into question whether Cobalt will pre-empt any agency action by launching its generic capsule prior to FDA making any decision on the exclusivity forfeiture. We also file this as a PSA to stay approval of any Cobalt ANDA or others.

Action Requested

Please stay Agency approval of any ANDA related to any generic ramipril capsule until a decision is made by the FDA and/or a court of law from which no further appeal may be taken.

Statement of Grounds

Under 21 C.F.R. 8 10.35(e), FDA must grant a stay of action if all of the following criteria are met:

(1) the petitioner will otherwise suffer irreparable injury;
(2) the petitioner's case is not frivolous and is being pursued in good faith;
(3) the petitioner has demonstrated sound public policy grounds supporting the stay; and
(4) the delay resulting from the stay is not outweighed by public health or other public interests.

Here it is plain that all criteria are satisfied. Apotex is one of many generic companies that have a clear interest in the proper resolution of exclusivity issues, especially where the FDA itself has invited comment. Apotex, among others, would be irreparably harmed by a pre-emptive strike because it might moot the Agency decision and thereby moot an important decision and the contributing jurisprudence. The PSA is not frivolous because it addresses precisely the very question the FDA invited companies, like Apotex, to opine. There are sound public policy grounds to support the stay for the very reasons the FDA opened the Docket in the first place. There is no prejudice to Cobalt because, as Apotex believes, it has nothing to delay. But the delay is important because it provides full clarity to the legal issues pronounced and opens the door to widespread generic competition that benefits the public. "The public's interest in 'the faithful application of the laws'outweigh[s] its interest in immediate access to [a competing] product." Mova Pharmaceutical Corp. v. Shalala, 140 F.3d 1060, 1066 (D.C. Cir. 1998). Cobalt cannot be heard to complain as it had received final launch approval, could have launched with the so-called 180-Day exclusivity, but did not do so. (See Exhibit 1 – Cobalt Approval letter dated 24 Oct. 2005). Cobalt settled its case months *later* on or about 04 April 2006.

Background

As you know, Cobalt was ostensibly the first to file against ramipril and challenge the patents, but laid down its sword to allow itself to be skewered by King Pharmaceuticals, the brand company. The current docket relates to whether voluntarily laying down on the battlefield and voluntarily being skewered still allows the victim to protest that he is still fighting the patent and thus can maintain its 180-Day exclusivity. For the reasons stated in the Docket by Apotex and others, one cannot charge the battlefield, beat its shield with the sword, and when the brand company attacks to then fall down, open yourself to attack, die on the sword, and then somehow (with a straight face) allege that you still have the fight left.

Alternatively, Cobalt cannot maintain its Paragraph IV certification because it is deemed converted to a Paragraph III or is deemed defective. It is well-established that an ANDA must be correct in all its constituents, including the patent certification section. The predicate is that the certification is correct. When it settled the lawsuit, Cobalt cannot maintain its Paragraph IV certification in good faith. Accordingly, the ANDA contains a material defect. No ANDA may be approved unless that material defect is cured. The cure is either a conversion of the Paragraph IV certification to Paragraph III (or II) or withdrawal of the Paragraph IV certification.

Knowing this, Cobalt is potentially planning to circumvent the FDA decision of Cobalt's death by launching something early.

According to King's recent 10-Q SEC filing, part of the Cobalt-King settlement agreement was that Cobalt would be the authorized generic for King. Apparently that agreement also stated that Cobalt could send a 30-Day notice letter to inform King that Cobalt intended to sell a generic product after that 30-Day notice. King apparently received that letter on or about 12 October 2007 and therefore, the 30-Day deadline is on or about 12 November 2007. (See Exhibit 2 – King's recent 10-Q, in relevant part).

According to King's 10-Q, "Pursuant to the dismissal agreement, on October 12, 2007, Cobalt sent the Company 30-day written notice of its intent to launch its generic ramipril product **which product would not be supplied by the Company**." As such, King does not intend to supply Cobalt with generic ramipril. Where will Cobalt get its products? It cannot be from its own ANDA because the FDA website lists the Cobalt ANDA as "DISCONTINUED." Therefore, because Cobalt has no approvable ANDA and that King is not intending to supply Cobalt, Cobalt cannot launch anything. To the extent Cobalt has something to launch, then clearly it is launching before FDA makes its decision on whether others can co-launch with Cobalt.

Currently Teva, Purepac, Sandoz, Roxane, and Dr. Reddy's have tentative approval and have a vested interest in knowing whether Cobalt is entitled to launch alone and enjoy the 180-Day exclusivity or whether these companies are entitled to compete head-to-head on Day 1 with Cobalt because Cobalt has no 180-Day exclusivity. (See Exhibit 3 – Copy of Approval website, visited 12 Nov. 2007). In addition, any pending ANDA applicant that is almost approvable has the right to know whether it will obtain tentative approval because FDA ruled that Cobalt has the 180-Day exclusivity or whether that company will receive full launch approval and enter the market at that time.

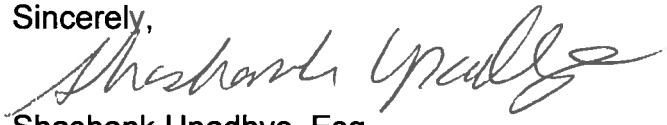
Or, Cobalt may intend to selectively waive its 180-Day exclusivity in favor of either Teva, Purepac, Sandoz, Roxane or Dr. Reddy so that any of those companies will launch and share royalties with Cobalt. In this regard, this is also wrong because the predicate to selective waiver is that there is something to waive. Until the FDA decides whether Cobalt has the 180-Day, there is nothing to selectively waive. Cobalt does not have an active ANDA pending and thus its only ability to get a product on the market is through King, which said it would not supply, or through a selective waiver, which does not apply since there is nothing to waive.

We therefore request that the FDA deny Cobalt any approvals to launch any generic product until the FDA makes an informed and timely decision on whether Cobalt forfeited or relinquished any 180-Day exclusivity it may have had.

Conclusion:

For the reasons set forth above, please take action in accordance with this.

Sincerely,



Shashank Upadhye, Esq.
Vice President – Global Intellectual Property
Apotex, Inc.
150 Signet Drive
Toronto, ON Canada M9L 1T9

Cc: Elizabeth Dickinson, Gary Buehler, Jeffrey Senger

Exhibit 1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

ANDA 76-549

OCT 24 2005

Strategic Bioscience Corporation
U.S. Agent for: Cobalt Pharmaceuticals, Inc.
Attention: James Parker, Ph.D.
93 Birch Hill Road
Stow, MA 01775

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 26, 2002, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ramipril Capsules, 1.25 mg, 2.5 mg, 5 mg, and 10 mg.

Reference is also made to your amendments dated May 29, 2003; October 22, and December 3, 2004; and February 9, March 31, May 2, and June 1, 2005. We also acknowledge receipt of your correspondence dated April 8, and August 18, 2003, pertaining to the patent issues associated with this ANDA.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the ANDA is approved. The Division of Bioequivalence has determined your Ramipril Capsules, 1.25 mg, 2.5 mg, 5 mg, and 10 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug Altace Capsules, 1.25 mg, 2.5 mg, 5 mg, and 10 mg, respectively, of King Pharmaceuticals, Inc. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

The referenced listed drug product (RLD) in your ANDA, Altace Capsules of King Pharmaceuticals Inc. (King), is subject to periods of patent protection. As noted in the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent 5,061,722 (the '722 patent) is scheduled to expire on October 29, 2008, and U.S. Patent 5,403,856 (the '856 patent) is scheduled to expire on April 4, 2012.

With respect to the '856 patent, your ANDA contains a statement under section 505(j)(2)(A)(viii) of the Act that the '856 patent is a method of use patent that does not claim a use for which you are seeking approval in this ANDA.

With respect to the '722 patent, your ANDA contains a paragraph IV patent certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Ramipril Capsules, 1.25 mg, 2.5 mg, 5 mg, and 10 mg under this ANDA. Section 505(j)(5)(B) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action was brought against Cobalt Pharmaceuticals, Inc. (Cobalt) for infringement of the '722 patent. This action must have been brought against Cobalt prior to the expiration of 45 days from the date the notice you provided under paragraph (2)(B)(i) was received by the NDA/patent holder(s). You have notified the agency that Cobalt complied with the requirements of section 505(j)(2)(B) of the Act, and that a patent infringement suit was initiated against Cobalt involving Ramipril Capsules, 1.25 mg, 2.5 mg, 5 mg, and 10 mg, with respect to the '722 patent (and the '856 patent) in the United States District Court for the District of Massachusetts (Aventis Pharma Deutschland GMBH and King Pharmaceuticals, Inc. v. Cobalt Pharmaceuticals, Inc., Civil Action No. 03-10492JLT). We acknowledge that the 30-month stay provided under section 505(j)(5)(B)(iii) of the Act expired on August 10, 2005.

With respect to 180-day generic drug exclusivity, we note that Cobalt was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Cobalt is eligible for 180-days of market exclusivity. This exclusivity, which is provided for under section 505(j)(5)(8)(iv) of the Act,[1] will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv). Please submit correspondence to the ANDA informing the agency of the date the exclusivity begins to run.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

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[1] Because your ANDA was filed before the date of enactment of the Medicare Prescription Drug, Improvement and Modernization Act (MMA)(Public Law 108-173) on December 8, 2003, this reference to the 180-day exclusivity provision is to the section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsvile, MD 20705-1266

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications (HFD-42) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Exhibit 2

more novel formulations of ramipril, the active ingredient in the Company's Altace® product. Under a series of agreements, Arrow has granted King rights to certain current and future New Drug Applications regarding novel formulations of ramipril and intellectual property, including patent rights and technology licenses relating to these novel formulations. Arrow will have responsibility for the manufacture and supply of the new formulations of ramipril for King. However, under certain conditions King may manufacture and supply the formulations of ramipril.

Upon execution of the agreements, King made an initial payment to Arrow of $35,000. During the fourth quarter of 2006 and the first quarter and second quarters of 2007, the Company made additional payments of $25,000 in each of the three quarters to Arrow. Additionally, Arrow will earn fees for the manufacture and supply of the new formulations of ramipril.

In connection with the agreement with Arrow, the Company recognized the above payments and future payments totaling $110,000 as in-process research and development expense during 2006. This amount was expensed as in-process research and development as the project had not received regulatory approval and had no alternative future use. The in-process research and development project is part of the branded pharmaceutical segment. This project includes a New Drug Application ("NDA") filed by Arrow for a tablet formulation of ramipril in January 2006 (the "Ramipril Application"). At the time of the acquisition, the success of the project was dependent on additional development activities and FDA approval. The estimated cost to complete the project at the execution of the agreement was approximately $3,500. The FDA approved the Ramipril Application on February 27, 2007. Arrow granted the Company an exclusive option to acquire their entire right, title and interest to the Ramipril Application or any future filed Amended Ramipril Application for the amount of $5,000. In April 2007, the Company exercised its option and paid $5,000 to Arrow. As a result, the Company owns the entire right, title and interest in and to the Ramipril Application. The Company expects to launch the tablet formulation during the fourth quarter of 2007.

On February 12, 2006, the Company entered into an agreement with Cobalt Pharmaceuticals, Inc. ("Cobalt"), an affiliate of Arrow International Limited, whereby Cobalt has the non-exclusive right to distribute a generic formulation of the Company's currently marketed Altace® product in the U.S. market, which generic product would be supplied by King. On October 12, 2007, Cobalt sent the Company 30-day written notice of its intent to launch its generic ramipril product, which product would not be supplied by the Company. The Company responded on October 19, 2007, informing Cobalt that the Company intends to vigorously enforce its rights under the '722 and '856 patents to the full extent of the law. For additional information, please see Note 8.

5. Intangible Assets and Goodwill

The following table reflects the components of intangible assets as of:

	September 30, 2007		December 31, 2006	
	Gross Carrying Amount	Accumulated Amortization	Gross Carrying Amount	Accumulated Amortization
Trademarks and product rights	$ 911,721	$ 385,612	$ 1,056,991	$ 337,046
Patents	538,183	232,259	272,833	202,873
Other intangibles	7,700	7,407	7,700	7,292
Total intangible assets	$ 1,457,604	$ 625,278	$ 1,337,524	$ 547,211

Amortization expense for the three months ended September 30, 2007 and 2006 was $26,749 and $26,836, respectively. Amortization expense for the nine months ended September 30, 2007 and 2006 was $81,044 and $79,380, respectively.

$49,800, plus interest from the date of the decision. The Company recorded approximately $45,100 in the fourth quarter of 2006 and had previously recorded $5,000 in 2004, related to this arbitration. In January

2007, the Company paid Elan approximately $50,100, which included interest of approximately $300.

Cobalt Pharmaceuticals, Inc. ("Cobalt"), a generic drug manufacturer located in Mississauga, Ontario, Canada, filed an Abbreviated New Drug Application ("ANDA") with the U.S. Food and Drug Administration (the "FDA") seeking permission to market a generic version of Altace®. The following U.S. patents are listed for Altace® in the FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* (the "Orange Book"): United States Patent No. 5,061,722 (the "722 patent"), a composition of matter patent, and United States Patent No. 5,403,856 (the "856 patent"), a method-of-use patent, with expiration dates of October 2008 and April 2012, respectively. Under the federal Hatch-Waxman Act of 1984, any generic manufacturer may file an ANDA with a certification (a "Paragraph IV certification") challenging the validity or infringement of a patent listed in the FDA's Orange Book four years after the pioneer company obtains approval of its New Drug Application ("NDA"). Cobalt filed a Paragraph IV certification alleging invalidity of the '722 patent, and Aventis Pharma Deutschland GmbH ("Aventis") and the Company filed suit on March 14, 2003 in the District Court for the District of Massachusetts to enforce the rights under that patent. Pursuant to the Hatch-Waxman Act, the filing of that suit provided the Company an automatic stay of FDA approval of Cobalt's ANDA for 30 months (unless the patents are held invalid, unenforceable, or not infringed) from no earlier than February 5, 2003. That 30-month stay expired in August 2005 and on October 24, 2005, the FDA granted final approval of Cobalt's ANDA. In March 2004, Cobalt stipulated to infringement of the '722 patent. Subsequent to filing its original complaint, the Company amended its complaint to add an allegation of infringement of the '856 patent. The '856 patent covers one of Altace®'s three indications for use. In response to the amended complaint, Cobalt informed the FDA that it no longer seeks approval to market its proposed product for the indication covered by the '856 patent. On this basis, the Court granted Cobalt summary judgment of non-infringement of the '856 patent. The Court's decision does not affect Cobalt's infringement of the '722 patent. The parties submitted a joint stipulation of dismissal on April 4, 2006, and the Court granted dismissal. Pursuant to the dismissal agreement, on October 12, 2007, Cobalt sent the Company 30-day written notice of its intent to launch its generic ramipril product which product would not be supplied by the Company. The Company responded on October 19, 2007, informing Cobalt that the Company intends to vigorously enforce its rights under the '722 and '856 patents to the full extent of the law.

The Company has received a civil investigative demand ("CID") for information from the U.S. Federal Trade Commission ("FTC"). The CID requires the Company to provide information related to the Company's collaboration with Arrow, the dismissal without prejudice of the Company's patent infringement litigation against Cobalt under the Hatch-Waxman Act of 1984 and other information. The Company is cooperating with the FTC in this investigation.

Lupin filed an ANDA with the FDA seeking permission to market a generic version of Altace® ("Lupin's ANDA"). In addition to its ANDA, Lupin filed a Paragraph IV certification challenging the validity and infringement of the '722 patent, and seeking to market its generic version of Altace® before expiration of the '722 patent. In July 2005, the Company filed civil actions for infringement of the '722 patent against Lupin in the U.S. District Courts for the District of Maryland and the Eastern District of Virginia. Pursuant to the Hatch-Waxman Act, the filing of the lawsuit against Lupin provided the Company with an automatic stay of FDA approval of Lupin's ANDA for up to 30 months (unless the patents are held invalid, unenforceable, or not infringed) from no earlier than June 8, 2005. On February 1, 2006, the Maryland and Virginia cases were consolidated into a single action in the Eastern District of Virginia. On June 5, 2006, the District Court granted King summary judgment and found Lupin to infringe the '722 patent. On June 14, 2006, during the trial, the District Court dismissed Lupin's unenforceability claims as a matter of law, finding the '722 patent enforceable. On July 18, 2006, the District Court upheld the validity of the '722 patent. Lupin filed a notice of appeal on July 19, 2006. All appellate briefing was completed as of March 19, 2007, and the Circuit Court heard oral arguments on July 12, 2007. On September 11, 2007, the Circuit Court reversed the decision of the

Exhibit 3

U.S. Food and Drug Administration

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Overview

Drug Name	**RAMIPRIL**
Active Ingredient(s)	**• RAMIPRIL**
Form(s) and Strength(s) Available	**• CAPSULE; ORAL: 1.25MG; 10MG; 2.5MG; 5MG**

Details about drugs are organized by FDA Application Number (NDA or ANDA or BLA).

Click on a drug name or application number to view drug details:

Click on a column header to re-sort the table:

Drug Name and FDA Application Number	Dosage Form/Route	Strength	Marketing Status	Comp
RAMIPRIL (ANDA # 076549)	CAPSULE; ORAL	Multiple Strengths	Discontinued	COBAL
RAMIPRIL (ANDA # 077470)	CAPSULE; ORAL	Multiple Strengths	None (Tentative Approval)	TEVA PHARM
RAMIPRIL (ANDA # 077513)	CAPSULE; ORAL	Multiple Strengths	None (Tentative Approval)	PUREF PHARM
RAMIPRIL (ANDA # 077514)	CAPSULE; ORAL	Multiple Strengths	None (Tentative Approval)	SANDC
RAMIPRIL (ANDA # 077900)	CAPSULE; ORAL	Multiple Strengths	None (Tentative Approval)	ROXAN
RAMIPRIL (ANDA # 078191)	CAPSULE; ORAL	Multiple Strengths	None (Tentative Approval)	DR REDDY LABS L

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FDA Approved Drug Products

Drug Details

Drug Name(s)	RAMIPRIL (Generic Drug)
FDA Application No.	(ANDA) 076549
Active Ingredient(s)	RAMIPRIL
Company	COBALT
Original Approval or Tentative Approval Date	October 24, 2005

- There are no Therapeutic Equivalents
- Approval History, Letters, Reviews, and Related Documents
- Labels are not available

Products on Application (ANDA) #076549

Click on a column header to re-sort the table:

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	RLD	TE Code
RAMIPRIL	RAMIPRIL	1.25MG	CAPSULE; ORAL	Discontinued	No	None
RAMIPRIL	RAMIPRIL	2.5MG	CAPSULE; ORAL	Discontinued	No	None
RAMIPRIL	RAMIPRIL	5MG	CAPSULE; ORAL	Discontinued	No	None
RAMIPRIL	RAMIPRIL	10MG	CAPSULE; ORAL	Discontinued	No	None

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