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Ambassador Michael Froman
United State Trade Representative
600 17th Street NW
Washington, DC 20508

Re: Indian compulsory licenses on dasatinib patents

October 29, 2014

Dear Ambassador Froman,

We represent the Union for Affordable Cancer Treatment (UACT) and more generally people who share the conviction that cancer drugs should be affordable and available to all.

We are writing because reports in Indian newspapers, television stations and blogs suggest that you, in your capacity as the head of the office of the United States Trade Representative (USTR), are pressuring the Indian government to deny patients access to affordable generic versions of dasatinib, a drug used to treat a rare form of leukemia.

The issue involves patents held by Bristol-Myers Squibb for a cancer drug, marketed by BMS under the trade name Sprycel, that treats both Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) and chronic myeloid leukemia (CML). Dasatinib is a critical drug that fills an important gap in treatment, particularly for patients who have developed a resistance to imatinib (a drug sold by Novartis under the trade names Gleevec or Glivec).

The BMS price for dasatinib in India is 6,627 rupees for a daily dose of 100 mg.[1] This is roughly $108 per day[2], for a country with a per capita income of just $1,570 per year, and where most patients pay for cancer drugs out of pocket. Companies seeking a compulsory license have

[1] 165,680 ruppes for 50mg x 50. (Enough for 25 days, at 100 mg per day). http://www.medindia.net/drug-price/dasatinib/sprycel-tab.htm.
[2] $39,480 per year, or more than 25 times the per capita income.

offered to supply generic versions of dasatinib for $4 per day[3], and that price would likely fall if competition was permitted.

In our view, opposition to the granting of a compulsory license in India is a *de facto* endorsement of excessive pricing, a rejection of the goal of access to medicine for all, and a death sentence for leukemia patients.

UACT recognizes that trade pressure on developing countries to make drug monopolies stronger and prices higher has been a longstanding objective of USTR, with bipartisan support in the U.S. Congress, but this should change, for a variety of reasons.

The first and most obvious shortcoming of the current policy is that high prices prevent most people in the world from having access to new live saving drugs, and this by itself should settle the question. But there are other reasons to reassess the decades old policy of advocating for higher and higher prices on drugs, vaccines and medical devices.

High drug prices create problems everywhere. In the United States, the negative impacts are several. First, high prices create access barriers for new medicines, often a consequence of restrictive reimbursement policies by governments, insurance companies and employers. Second, high drug prices drive up the costs of taxes, insurance and out-of-pocket costs to patients. Third, since employers pay for taxes and often directly or indirectly for the costs of drugs for their own employees, higher prices in the United States make the U.S. workforce less competitive in global markets, and encourages the outsourcing of U.S. jobs.

When it comes to cancer drugs, the United States has a strong interest in controlling the cost of new life saving drugs. While cancer affects people of all ages, the probability of having cancer is much higher for older persons. According to the NIH's National Cancer Institute (NCI), the rate of incidence for cancer is seven times higher for the 65 and older population, than the population under 65 years old. The World Bank estimates that 8 percent of the world population is 65 or older. But in the United States in 2011, 12.8 percent of the population was 65 or older. According to the U.S. Administration on Aging, by 2020 more than 16 percent of the U.S. population will be 65 or over, and by 2030, the percentage will be 19.3 percent.

If drug prices are not lowered, people living in the United States will face greater restrictions on reimbursements and higher out of pocket costs, and U.S. employers will become less competitive globally (because of the higher taxes and insurance costs associated with paying for those drugs).

Furthermore, the BMS drug Sprycel provides a textbook case of abusive and unjustified pricing policies, in India, but also in the United States.

[3] Indian Health Ministry seeking compulsory license for BMS's Sprycel. *The Pharma Letter.* August 19, 2014.

The development of Sprycel began with extensive U.S. taxpayer investments in research on leukemia, and on the cancer fighting properties of tyrosine-kinase inhibitors. This research led to the development of three drugs, imatinib, nilotinib and dasatinib to treat CML and ALL.

imatinib and nilotinib

The first tyrosine-kinase inhibitor used to treat CML and ALL was imatinib, approved by the FDA in May 2001. According to the scientist Brian Druker, about 90 percent of the pre-clinical research on imatinib was financed by the NIH, private charities and his university. Much has been written about the relative role of the public and private sector in the development of imatinib. One estimate is that the Novartis out-of-pocket outlays on clinical studies were $10 to $24 million. When adjusted for risks of failures and capital costs, the estimate is in the range of $38 to $96 million.[4]

In 2007, following the BMS registration of dasatinib, Novartis registered nilotinib (trade name Tasigna). Nilotinib, like dasatinib, is used when a patient develops resistance to imatinib. Nilotinib was approved based upon evidence from 438 patients, less than 10 percent of the "average" number of patients in trials cited by various drug company funded studies of drug development costs.

Novartis received 7 separate Orphan Drug designations for imatinib and 2 designations for nilotinib, each allowing Novartis to claim a 50 percent credit against the costs of clinic trials.

Despite the modest costs associated with the development of both drugs, and the extent of US R&D subsidies, Novartis is aggressive in its pricing of both drugs. In 2001, when first registered, the price of Gleevec was about $80 per day for 400 milligrams. Today the U.S. price of Gleevec is $287 per day, for the same dose, and the current U.S. price for nilotinib is $318 per day.

Prices for imatinib/Gleevec and nilotinib/Tasigna are considerably lower outside of the United States. For example, a 400 mg dose of Gleevec ($287 in the United States) is $111 in Australia. $93 in the UK, $130 in Denmark and $106 in the Netherlands. Nilotinib ($318 in the United States) is $131 in Australia, and $140 in the UK.

In 2013 Novartis reported sales of $4.693 billion for imatinib, plus $1.266 billion in additional revenues for nilotinib, or $5.959 billion for both products.

[4] R&D costs for Gleevec. April 2013. http://www.keionline.org/node/1697

Development and price of dasatinib

Registered with the FDA in 2006, dasatinib was the second tyrosine-kinase inhibitor approved by the FDA for the treatment of leukemia. Like imatinib and nilotinib, R&D outlays for dasatinib were modest. According to a study by Jacqueline Lee, the estimated out-of-pocket cost of the clinical studies used in the 2006 FDA approval were in the range of $7 to $26 million. Dasatinib qualified for the Orphan Drug tax credit for trials involving both CML and ALL.

The roles of the NIH and non-profit organizations in the development of these drugs were extensive, a fact illustrated by the 2009 Lasker~DeBakey Clinical Medical Research Award[5], which honored three scientists, two of which worked at academic institutions, Brian Druker[6], for his role in the development of imatinib, and Charles Sawyers[7], for his role in the development of dasatinib. The federal government's role included not only extensive grant support for academic researchers, but also direct sponsoring and funding of clinical trials, as well as the 50 percent tax credit for the trials sponsored by BMS .

Much like Novartis, BMS has been aggressive with regard to the price of its leukemia drug. In 2006, Dasatinib was priced at $156 per day, for a dose of 2 x 70mg per day. When the FDA subsequently recommended a lower dose of 100mg per day, BMS responded with a 100 mg tablet priced at $200. Today, that 100mg tablet has an average U.S. wholesale price of $367. Prices for dasatinib are considerably lower in other countries. For a 100mg tab, the price is $147 in Australia, $134 in the UK, $150 in Canada, $172 in the Netherlands, and $147 to $188 in Norway.

dasatinib in India

The BMS price for dasatinib in India is 165,680 rupees for 50 x 50mg tabs.[8] A daily dose of 100mg is 6,627.2 rupees, $108 at current exchange rates, and 25 times the average incomes in India.

The Indian Ministry of Health has requested that the Department of Industrial Policy and Promotion (DIPP) issue a compulsory license for dasatinib. The DIPP is reportedly opposing the compulsory license, motivated primarily by concerns that a compulsory license would create trade and foreign policy problems with the United States.

The decision to put off judgement on issuing a compulsory license came during a period when the USTR officials have criticized the Indian government over two other disputes involving drug

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[5] http://www.laskerfoundation.org/awards/2009_c_description.htm

[6] Oregon Health & Science University. Druker is names as a principal investigator or project leader for 59 NIH funded projects, and 80 NIH funded sub-projects.

[7] Memorial Sloan-Kettering Cancer Center. Charles Sawyers is named as a principal investigator or project leader for 34 NIH funded projects, and 16 NIH funded sub-projects.

[8] http://www.medindia.net/drug-price/dasatinib/sprycel-tab.htm

patents, including the US government criticism of the rejection of the Novartis evergreening patents on imatinib, and US government criticism of the Comptroller of Patent's decision to grant a compulsory license on Bayer's patents on sorafenib, a $65,000 per year drug for kidney and liver cancer.

According to various news reports and Congressional testimonies, you, deputy USTR Wendy Cutler, other officials from USTR, the President of the United States, Vice President Joe Biden, Secretary of State John Kerry, Secretaries Commerce and the head of the US patent office have all engaged India on its patent policies, as have Congressional Committees and the United States International Trade Commission (USITC). India is also the target of a USTR out-of-cycle review of India's status on the Special 301 Report.

These and other actions represent a clear and concerted effort on the part of the USTR and the larger executive branch to put pressure on the Indian government, and to influence the intellectual property policy of India in such a way as to severely restrict access to newer medicines for cancer patients.

We are writing today both to ask for clarification regarding the extent to which the USTR is actively discouraging the granting of a compulsory licenses on the dasatinib patents (or other cancer drug patents), but also to suggest that it is time for the United States to change our trade policies as regard innovation and access to new cancer drugs.

At present, the USTR has a simple policy regarding cancer drugs -- to make them as expensive as possible everywhere in the world. This extends even to the United States, as USTR is advocating for provisions in the TPP trade agreement that will make it impossible to reform US laws on test data exclusivity for biologic drugs, expand evergreening of patents, and make it more costly and difficult to grant compulsory licenses on drug patents.

If the USTR objectives in India are to reduce the number of compulsory licenses, and to prevent developing countries from sourcing generic cancer drugs from India, then it is going to extremes and systematically ending any hope for cancer patients to live longer and better lives.

For leukemia patients, high drug prices are the problem and not the solution. Low drug prices are a desired outcome, not a threat.

In the United States, there are consequences of $100,000 and higher prices for cancer drugs, including restricted access[9], crushing co-payments, and a less competitive US workers and businesses, and in the absence of policy changes, these problems are only going to get worse, given projected demographic changes.

[9] Including less access to off-label use for super expensive drugs, eliminating opportunities for patients with failing treatments to experiment.

The United States may, to some extent, succeed in getting other countries to pay higher prices for drugs, but it is highly likely the United States will continue to pay the higher cancer drug prices, causing unnecessary death, pain and bankruptcy (referred to as financial toxicity in a recent 60 minutes program[10]) in the United States, and leading to a less competitive workforce.

The United States must push back on high drug prices. Dasatinib/Sprycel is a case in point. The Sprycel price per milligram has more than tripled since the the registration of the drug, and US consumers are paying two to three times more than other higher income countries, for a drug developed with U.S. government R&D subsidies.

One way that governments can push back on the high drug prices is to refuse to reimburse the drug. That is the approach that many governments have taken. For example, in the UK, a review by NICE in 2012 found that "dasatinib [was] more effective than imatinib. But it could not recommend dasatinib because . . . its high cost did not justify the benefits provided."[11] Even those governments that do reimburse dasatinib, do so only in limited cases that are more restrictive than the medical needs. UACT is opposed to governments relying upon threats to restrict cancer patient access as a mechanism to control drug prices.

A different way to push back on high drug prices is to directly regulate the prices of drugs, or to impose sanctions when prices are excessive. One powerful way to impose sanctions on unreasonable prices, or more generally to protect the interests of consumers, is to eliminate the legal monopoly on a product, such as by granting compulsory licenses on patents, or to limit the remedies for infringing a patent. We note that in an August 3, 2013 letter to US ITC Chairman Irving Williamson, you cited the legislative history of Section 337 of the trade act to overturn an injunction on the importation of Apple smart phones and tablets that infringed patents held by Samsung.[12] This same authority should be used to permit the importation of affordable generic drugs. The threat of doing so would clearly have a first order impact on the prices of drugs in the United States, as was the case in 2001, when the U.S. government used the threat of a compulsory license to cut by 50 percent the price of ciprofloxacin, to address a health crisis that involved the death of five persons.

By taking a holier than thou or maximalist approach on intellectual property rights in trade negotiations, USTR necessarily makes it more difficult for other U.S. federal or state government agencies to explore the limitations on patent rights needed to address the current crisis in the pricing of drugs in the United States. Governments need to expand rather than restrict access to newer life saving drugs.

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[10] Lesley Stahl, The cost of cancer drugs, 60 minutes, October 5, 2014. http://www.cbsnews.com/news/the-cost-of-cancer-drugs/

[11] Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia. http://www.nice.org.uk/guidance/ta251

[12] http://www.ustr.gov/sites/default/files/08032013%20Letter_1.PDF

Concerns about R&D investments for new drugs are important, and UACT is fully committed to robust funding of innovation for new treatments and diagnostics for cancer. However, in this regard, pushing only for higher drug prices is a flawed approach. USTR and other federal agencies need to make the funding of global R&D the focus of negotiations, and to acknowledge that high prices on life saving drugs are a very limited and costly way to induce investments in medical R&D.

Perhaps you can ask your staff the following questions: Which negotiating objective is consistent with both innovation and access, and human rights, and U.S. national interest, given the shifting demographics in the United States, and which one is likely to be sustainable? (1) Asking India to forgo compulsory licenses on a cancer drug that costs $108 per day, in India, or (2) asking India to expand its public sector outlays in cancer research? Should we be asking our trading partners in high income countries to raise the price of dasatinib to $367 per day, or asking that they expand public sector funding of R&D?

Finally, should we begin to confront the fundamental and historic flaw in policy that links R&D funding to drug prices, in a world with immense suffering, and huge disparities of incomes? Are we willing to acknowledge the high cost of the current system, that returns just 8 cents per dollar of global sales in R&D, and which often wastes much of that 8 percent on medically unimportant R&D projects?

Spending your time opposing access to affordable dasatinib for leukemia patients in India is a poor use of your time and your negotiating skills.

We request a meeting with you to discuss these issues further.

Sincerely,

Manon Anne Ress
UACT

cc: Smt. Nirmala Sitharaman
Minister of State for Commerce and Industry
c/o mincom@indiagov.org

cc: Susan Wilson, USTR
cc: Shira Perlmutter, USPTO

Table 1: Age distribution of population, 2013 (Source World Bank).

Country	Ages 65+	Ratio of age 65+ to age 15- 64
Brazil	8	11
China	9	12
India	5	8
Japan	25	41
United States	**14**	**21**
World	**8**	**12**
Low income	4	7
Middle income	7	10
Lower middle income	5	8
Upper middle income	8	12
Low & middle income	6	9
East Asia & Pacific	8	11
Europe & Central Asia	10	15
Latin America & Caribbean	7	11
Middle East & North Africa	5	8
South Asia	5	8
Sub-Saharan Africa	3	6
High income	16	24
Euro area	19	29

Table 2: Older Population as a Percentage of U.S. Total Population: 1900 to 2050, Source: U.S. Administration on Aging

Census Year	Age 60 and older	Age 65 and older
1900	6.4%	4.1%
1910	6.8%	4.3%
1920	7.5%	4.7%
1930	8.5%	5.4%
1940	10.4%	6.8%
1950	12.2%	8.1%
1960	13.2%	9.2%
1970	14.1%	9.9%
1980	15.7%	11.3%
1990	16.8%	12.6%
2000	16.3%	12.4%
2010	18.4%	13.0%
2020	22.2%	16.1%
2030	24.7%	19.3%
2040	25.1%	20.0%
2050	25.5%	20.2%