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Written Submission of Knowledge Ecology International to the Senate Committee on Health Care on SB793

Knowledge Ecology International (KEI) appreciates the opportunity to submit these written comments on SB 793, which creates a mechanism for the Oregon Department of Consumer and Business Services to investigate increases in the prices of prescription drugs in the State of Oregon.

KEI is a non-profit non-governmental organization based in Washington, D.C., that advocates for access to affordable medicines, with a focus on social justice and human rights. KEI has an interest in legislation that improves transparency in the pharmaceutical sector, from the local to the international level. Transparency legislation benefits consumers and researchers who are seeking change in the way that we finance and conduct research and development.

With regards to SB 793, KEI supports the requirement of the department to evaluate "The direct costs incurred by the manufacturer," § 1(4)(a), which includes the costs incurred "In the research and development of the prescription drug" § 1(4)(a)(A), when determining whether a price increase is excessive.

However, KEI also recommends an amendment to the bill to require an **increased level of detail of research and development costs**, particularly as they relate to clinical trials. KEI also recommends that the Committee ensure that such information that is collected in the course of an investigation under this act is **easily and publicly available**. Our proposed amendment is attached to this testimony as Appendix 1.

The Act should require the disclosure and evaluation of the cost of **each clinical trial**, separated by phase and year, that was used to support the approval of the drug by the United States Food and Drug Administration, rather than an aggregate cost of all clinical trials or the total cost of research and development.

Clinical trial costs are the most expensive part of drug research and development. But, when pharmaceutical companies provide an aggregated “total” clinical trial cost, they often include risk adjustments, without providing an explanation of their economic assumptions, and the costs of acquiring patent licenses or other data unrelated to the costs of conducting a trial. The Department, in conducting an investigation under this Act, should have the authority and ability to verify whether the total research and development cost for a prescription drug matches up with the costs for each trial and with reasonable assumptions about the per patient cost of a clinical trial.

The public should also have access to any data collected regarding the costs of clinical trials in order to independently verify the work of the Department and conduct additional research related to the costs of clinical trials, as well as the prices of drugs.

Moreover, research and development costs should not be considered “trade secrets” within the scope of § 1(7) of the Act and relevant Oregon law. Drug companies, particularly small firms, regularly disclose individual clinical trial costs, disaggregated by year and phase, in their filings with the United States Securities and Exchange Commission. Please see the attached Appendix 2 for examples of the various levels of detail that drug developers go into when they disclose clinical trial costs to investors.

Thank you again for the opportunity to submit this testimony.

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Appendix 1: Proposed Amendments to SB 793

- Amend § 1(4)(a)(A) to read as follows:

  (A) In the research and development of the prescription drug, including:

  (i) The cost of each clinical trial cited by the United States Food and Drug Administration Medical Review for the approval of the relevant indication of the prescription drug, separated by year;

  (ii) The number of patients involved in each clinical trial, identified by the trial's identifier number on clinicaltrials.gov, prior to FDA approval of the first marketing indication, and the per patient cost for each clinical trial; and

  (iii) The amount of each subsidy received by the manufacturer, including but not limited to each federal, state, or other government grant, identified by the appropriate grant number and grant period, by year, and each tax credit, such as the United States orphan drug tax credit defined at 26 U.S.C. 45C;

- At the end of § 1(7), add the following sentence:

  The costs associated with the research and development of the prescription drug, as specified in § 1(4)(a)(A), shall not qualify as a trade secret.

- Renumber section 3 and section 4 to section 4 and section 5, respectively, and add the following new section 3:

  SECTION 3. The Department shall, after the closure of any inquiry conducted under sections 1 and 2 of this 2017 Act, make available upon request and on its website the results of any investigation, as well as any data, documents, or testimony collected pursuant to this 2017 Act.

Appendix 2: SEC Filing Examples
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Examples of Pharmaceutical Company R&D Cost Disclosures in SEC Filings

Introduction

There is significant diversity in how companies report R&D outlays to investors in their SEC filings. The purpose of the SEC filings is to provide information material to the price of a security to investors. In all cases, the companies report R&D outlays, but the level of detail varies. In general, the level of reporting is more detailed for smaller firms than for larger firms.

In some cases, companies report spending on specific trials, in other cases on specific drugs, and for other companies, the R&D spending is reported as a single line item, without elaboration on the allocation to products.

A number of firms include outlays related to the acquisition of licenses and other assets as research and development costs.

The following are a few examples of how companies report R&D spending to the SEC.

Clovis Oncology, Inc., 2016 10-K Filing

Clovis Oncology received FDA approval for Rubraca (INN: rucaparib), an ovarian cancer drug, on December 19, 2016. In its 2016 10-K report to investors, Clovis reports its R&D outlays for specific products, by year, as well as a general category for joint costs that are not allocated to specific products. Clovis reports separately the “acquired in-process” R&D from other R&D expenses.

	Year Ended December 31,		
	2016	2015	2014
Rucaparib Expenses	(In thousands)		
Research and development	$ 101,598	$ 58,922	$ 35,010
Acquired in-process R&D	1,300	—	400
Rucaparib Total	102,898	58,922	35,410
Lucitanib Expenses			
Research and development (a)	(1,337)	1,923	(491)
Acquired in-process R&D	—	—	3,406
Lucitanib Total	(1,337)	1,923	2,915
Rociletinib Expenses			
Research and development	43,768	122,912	69,920
Acquired in-process R&D	—	12,000	5,000
Rociletinib Total	43,768	134,912	74,920
Personnel and other expenses	107,100	85,494	33,266
Total	$ 252,429	$ 281,251	$ 146,511
(a)This amount reflects actual costs incurred less amounts due from Servier for reimbursable development expenses pursuant to the collaboration and license agreement described in Note 11, License Agreements, to our audited consolidated financial statements included in this Annual Report on Form 10-K.			

On July 31, 2012, the Food and Drug Administration granted Clovis an orphan designation for rucaparib, which entitled the company to a tax credit equal to 50 percent of the costs of the trials on that drug, from July 13, 2012 to the FDA approval on December 19, 2016. We do not know from SEC filings how much of a subsidy the company received from the orphan drug tax credit. Clovis also received an orphan designation for rociletinib on May 14, 2013.

Ionis Pharmaceuticals, 2015 10-K Filing

Inois Pharmaceuticals reports its "discovery" and "development" expenses for antisense drugs separately.

Our antisense drug discovery expenses were as follows (in thousands) and are part of our Ionis Core business segment:

	Year Ended December 31,	
	2015	2014
Antisense drug discovery expenses	$ 49,331	$ 43,620
Non-cash compensation expense related to equity awards	11,914	7,290
Total antisense drug discovery expenses	$ 61,245	$ 50,910

Antisense drug discovery expenses for 2015 were $49.3 million, and were slightly higher as expected, compared to $43.6 million for 2014. Expenses were higher because we conducted more research activities to support our partnerships in 2015 compared to 2014. All amounts exclude non-cash compensation expense related to equity awards.

The development costs for major antisense drug development projects are reported as separately.

Antisense Drug Development

The following table sets forth research and development expenses for our major antisense drug development projects (in thousands):

	Year Ended December 31,	
	2015	**2014**
Nusinersen	$ 35,164	$ 19,064
Volanesorsen	21,348	9,337
IONIS-TTRRx	19,560	10,927
Other antisense development projects	60,028	50,272
Development overhead expenses	36,117	31,318
Total antisense drug development, excluding non-cash compensation expense related to equity awards	172,217	120,918
Non-cash compensation expense related to equity awards	16,208	9,640
Total antisense drug development expenses	$ 188,425	$ 130,558

Antisense drug development expenses were $172.2 million for 2015, compared to $120.9 million for 2014. Expenses for 2015 were higher compared to 2014 primarily due to the progression of our drugs currently in Phase 3 trials. As drugs move forward to more advanced stages of development, including into larger, longer clinical studies, the costs of development increase. All amounts exclude non-cash compensation expense related to equity awards.

Ionis received an orphan designation for nusinersen on April 18, 2011, and for volanesorsen on June 23, 2015. Expenses related to clinical trials for that drug that occur after a designation and until the FDA approves the drug for the Orphan indication are eligible for a 50 percent tax credit from the IRS. The Orphan Drug tax credit is available even if a drug is is never approved by the FDA for the Orphan designation.

Anacor Pharmaceuticals, 2015 10-K Filing

Anacor Pharmaceuticals received FDA approval for the atopic dermatitis drug Eucrisa (INN: crisaborole) on December 14, 2016. Before its acquisition by Pfizer in 2016, Anacor filed its own SEC reports. This is from the 2015 10-K report:

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The table below presents our research and development expenses for the years ended December 31, 2015, 2014 and 2013, related to crisaborole, KERYDIN, work conducted under our Gates Foundation and DTRA programs and work on our other research programs (including early-stage research programs, neglected disease initiatives and AN3365, as well as our collaborations with GSK and Lilly). A portion of our research and development costs, including indirect costs, are not recorded on a program-by-program basis and are allocated based on the personnel resources assigned to each program.

	Year Ended December 31,		
	2015	**2014**	**2013**
	(in thousands)		
Crisaborole	$ 44,994	$ 41,680	$ 15,862
KERYDIN	5,015	13,040	15,279
Gates Foundation	5,792	6,608	5,085
DTRA	3,922	3,153	487
Other research programs	14,134	8,012	9,848
Total research and development expenses	$ 73,857	$ 72,493	$ 46,561

Sarepta Therapeutics, 2016 10-K Filing

Sarepta Therapeutics received FDA approval for Exondys 51 (INN: eteplirsen) on September 19, 2016, as a treatment for Duchenne muscular dystrophy. The *Rare Disease Report* estimated the annual price per patient at approximately $300,000.[1] In this table from the 10-K report, the company reports its R&D outlays on Exondys 51, as well as two other projects, Exon 45 and Exon 53.

The following table summarizes our research and development expenses by project for each of the periods indicated:

For the Year Ended December 31				
	2016	2015		2014
	(in thousands)			
EXONDYS 51 (exon 51)	$ 65,454	$ 72,147		$ 29,395
Exon 45	9,562	6,649		4,343
Exon 53	11,847	5,583		8,013
Other projects	1,248	2,178		4,196
Up-front and milestone payments	48,035	165		—
Internal research and development expenses	52,126	59,672		48,284
Total research and development expenses	$ 188,272	$ 146,394		$ 94,231

Sarepta earned an orphan drug designation for eteplirsen on October 23, 2007, making the trials eligible for a 50 percent tax credit for all of the clinical trials. In addition, the FDA awarded Sarepta a "Rare Pediatric Disease Priority Review Voucher (PRV)", which is an incentive for developing drugs that treat rare pediatric diseases. Sarepta sold the PRV to Gilead for $125 million.[2] The combined value of the PRV and the Orphan Drug Tax Credits exceeded the R&D outlays on the Exondys 51 from 2014 to 2016.

[1] Andrew Black and James Radke, "Sarepta's Duchenne Drug to Cost $300k Annually," *Rare Disease Report*, Sept. 19, 2016, http://www.raredr.com/news/duchenne-drug-to-cost-300k.
[2] Sarepta Sells Priority Review Voucher to Gilead for $125M, Genetic Engineering & Biotechnology News, February 21, 2017. http://www.genengnews.com/gen-news-highlights/sarepta-sells-priority-review-voucher-to-gilead-for-125m/81253908

The Sarepta 10-K report also broke down, for the company as a whole, the amount of the R&D spending that was associated with Clinical and manufacturing expenses. This was $82,077 for 2016, or 44 percent of R&D costs claimed for that year. Some other claimed costs are not necessarily related to R&D activities, including $48 million in "Up-front and milestone payments" in 2016 (26 percent of total R&D outlays for that year) and "Stock-based compensation" of $9.5 million.

The following table summarizes our research and development expenses by category for each of the periods indicated:

	For the Year Ended December 31		
	2016	2015	2014
	(in thousands)		(in thousands)
Clinical and manufacturing expenses	$ 82,077	$ 80,977	$ 39,505
Up-front and milestone payments	48,035	165	----
Compensation and other personnel expenses	21,322	25,746	20,234
Stock-based compensation	9,499	10,403	8,269
Facility-related expenses	8,095	9,919	7,792
Professional services	7,537	8,329	7,689
Preclinical expenses	3,415	3,948	2,758
Restructuring expenses	2,013	—	—
Research and other	6,279	6,907	7,984
Total research and development expenses	$ 188,272	$ 146,394	$ 94,231

Research and development expenses for 2016 increased by $41.9 million, or 29%, compared to 2015. The increase was primarily driven by increases of $47.5 million in up-front and milestone payments related to the Collaboration Agreement with Summit and the Amended and Restated UWA License Agreement and its First Amendment with UWA, $2.0 million in restructuring expenses, and $1.1 million in clinical and manufacturing expenses due to increased patient enrollment in our ongoing clinical trials . . .

The Sarepta filing also reports grants from governments the company has received to fund the R&D for Exon 53 and Exon 45.

Exon 53. . . . The SKIP-NMD Consortium, which supported certain clinical proof of concept studies and IND-enabling activities for an exon 53-skipping therapeutic using our PMO technology, received an EU Health Innovation-1 2012 collaborative research grant (grant agreement No. 305370) to support the initial development of SRP-4053. SRP-4053 will potentially address one of the most prevalent sets of mutations in DMD that are amenable to exon-skipping.

Exon 45. . . . SRP-4045, an exon 45-skipping product candidate that we selected for development in collaboration with Children's National Medical Center ("CNMC") in Washington, D.C. and the Carolinas Medical Center ("CMC") in Charlotte, N.C. This collaboration was funded primarily through two grants, one from Department of Defense's ("DoD") Congressionally Directed Medical Research Program to CNMC and the other from the National Institutes of Neurological Disorders and Stroke to the CMC. . . .

AMGEN 2016 10-K

Amgen report R&D costs by three stages.

The Company groups all of its R&D activities and related expenditures into three categories: (1) Discovery Research and Translational Sciences (DRTS), (2) later-stage clinical programs and (3) marketed products. These categories include the Company's R&D activities as set forth in the following table:

Category	Description
DRTS	R&D expenses incurred in activities substantially in support of early research through the completion of phase 1 clinical trials. These activities encompass our DRTS functions, including drug discovery, toxicology, pharmacokinetics and drug metabolism, and process development.
Later-stage clinical programs	R&D expenses incurred in or related to phase 2 and phase 3 clinical programs intended to result in registration of a new product or a new indication for an existing product in the United States or the EU.
Marketed products	R&D expenses incurred in support of the Company's marketed products that are authorized to be sold in the United States or the EU. Includes clinical trials designed to gather information on product safety (certain of which may be required by regulatory authorities) and their product characteristics after regulatory approval has been obtained, as well as the costs of obtaining regulatory approval of a product in a new market after approval in either the United States or the EU has been obtained.

According to Amgen, $1.747 billion of its 2016 R&D outlays, or 45 percent, were on “marketed products.” 27 percent were for Discovery Research and Translational Sciences (DRTS), and another 27 percent is spent on later-stage clinical programs.

Years ended December 31,			
	2016	2015	2014
DRTS	$ 1,039	$ 997	$ 1,212
Later-stage clinical programs	1,054	1,876	2,287
Marketed products	1,747	1,197	798
Total R&D expense	$ 3,840	$ 4,070	$ 4,297

A number of the Amgen products have benefited from federal research subsidies, including research grants from various federal agencies and the Orphan Drug Tax Credit, but these subsidies are not reported in the 10-K report. For example, these are among the Amgen products that have benefited from the Orphan Drug tax credit.

Selected Amgen products with Orphan Drug designations

Generic Name	Orphan Designation	Designation Date	Designation Status
blinatumomab	Treatment of acute lymphocytic leukemia	05/16/2008	Designated/Approved
carfilzomib	Treatment of multiple myeloma	01/18/2008	Designated/Approved
etanercept	Reduction in signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs.	10/27/1998	Designated/Approved
evolocumab	Treatment of homozygous familial hypercholesterolemia	09/12/2013	Designated/Approved
denosumab	Treatment of hypercalcemia in malignancy	09/11/2013	Designated/Approved
denosumab	Treatment of patients with giant cell tumor of bone	12/20/2010	Designated/Approved
talimogene laherparepvec	Treatment of stage IIb-stage IV melanoma	03/14/2011	Designated/Approved
Pegfilgrastim	Treatment of subjects at risk of developing myelosuppression after a radiological or nuclear incident	11/20/2013	Designated/Approved

oprozomib	Treatment of multiple myeloma	10/28/2014	Designated
oprozomib	Treatment of Waldenstrom's macroglobulinemia	08/25/2014	Designated

Bristol-Myers Squibb, 2016 10-K Filing

The Bristol-Myers Squibb (BMS) SEC filings claim “license and asset acquisition charges” as R&D expenses. This introduces an element of confusion, because the acquisition costs are unrelated to the money spent on R&D.

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> License and asset acquisition charges were $439 million in 2016, $1.7 billion in 2015 and $278 million in 2014 including $374 million for Padlock, Nitto Denko, Flexus and Cormorant in 2016, $1.3 billion for Flexus, Cardioxyl and Five Prime in 2015 and $148 million for iPierian in 2014. A $100 million milestone was paid to former shareowners of Flexus for the commencement of a Phase I clinical trial in 2016.

Pfizer 2016 10-K

The 2016 Pfizer 10-K report includes an exhibit 13, which is the Pfizer Inc. 2016 Financial Report:

The only detail regarding spending on specific products is the section of on “Our Business Development Initiatives,” pages 11-13 of the exhibit. Like other firms, Pfizer claims as R&D the costs associated with the acquisition of assets. For example, in discussion of collaboration with Merck KGaA, Pfizer says its R&D expenses included payments “reflecting the fair value of the co-promotion rights given to Merck KGaA.”

> Page 13.
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> Also, as part of the agreement, we gave Merck KGaA certain co-promotion rights for Xalkori in the U.S. and several other key markets, and co-promotion activities were initiated in key select markets in 2015. In 2014, we recorded $1.2 billion of *Research and development expenses* associated with this collaborative arrangement, composed of the $850 million upfront cash payment as well as an additional amount of $309 million, reflecting the estimated fair value of the co-promotion rights given to Merck KGaA.

Similar payments were reported involving the Pfizer collaboration with OPKO Health and the license with Cellectis to develop Chimeric Antigen Receptor T-cell immunotherapies.

The fact that BMS, Pfizer and other companies are reporting R&D outlays based upon the costs of acquiring of licenses and other assets creates a fog that obscures the actual costs of conducting research and development.

Comments

When it matters to investors, companies disclose R&D costs in significant detail. But the reporting varies in detail and focus from company to company, is very general for the largest companies, and does not present information in ways that are suited to evaluating the risk and subsidy adjusted costs of drug development.

Some of the industry reporting to investors obscures the actual costs of conducting R&D, by including the costs of acquiring licenses and other assets as research costs, when the costs of acquiring the assets are unrelated to costs of conducting research.