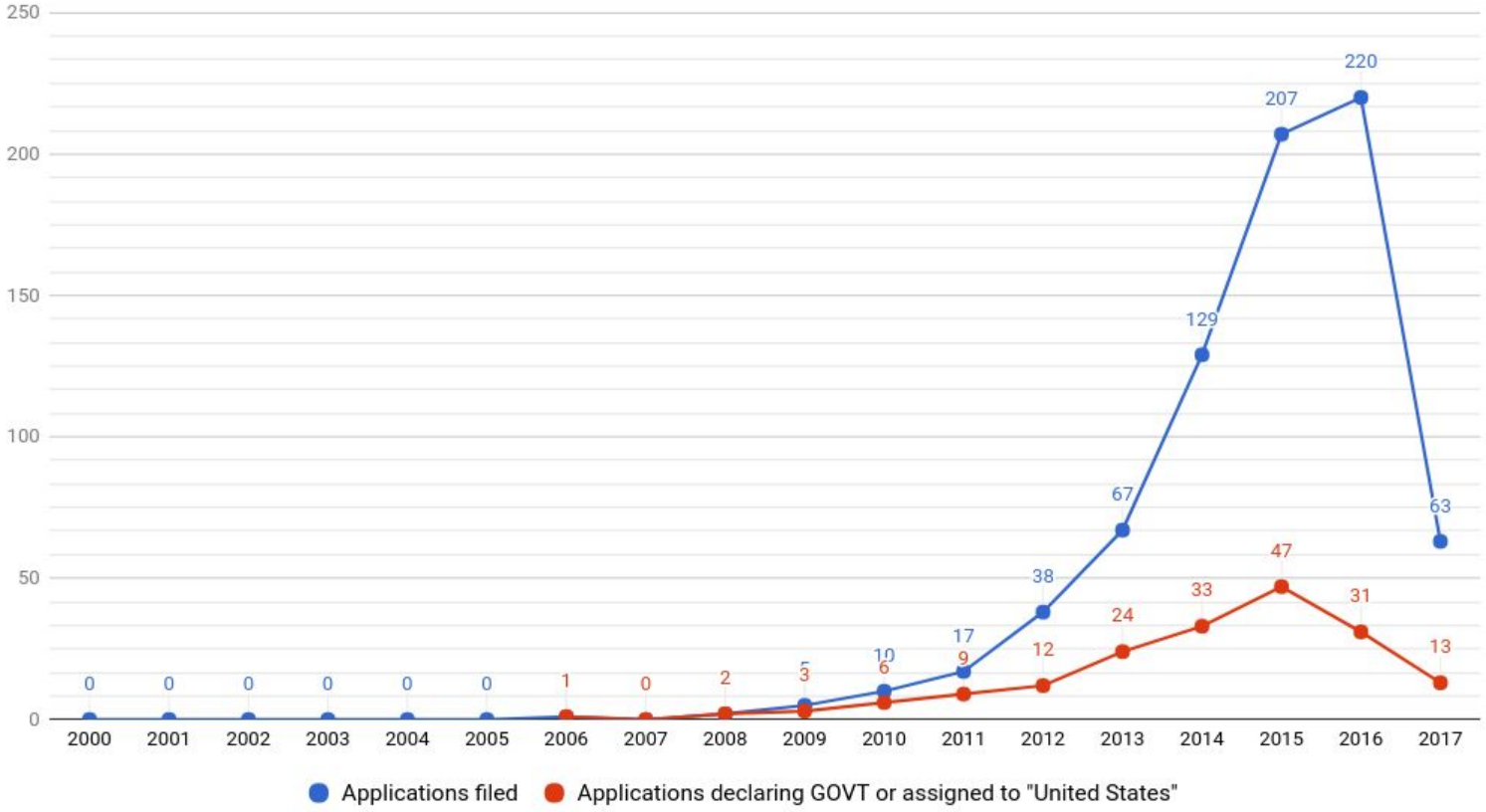
CAR T

Patents, the public and the public interest

James Love
KEI
September 15, 2017

Some data on CAR patents

USPTO Patent applications filed that mention "chimeric antigen receptor"

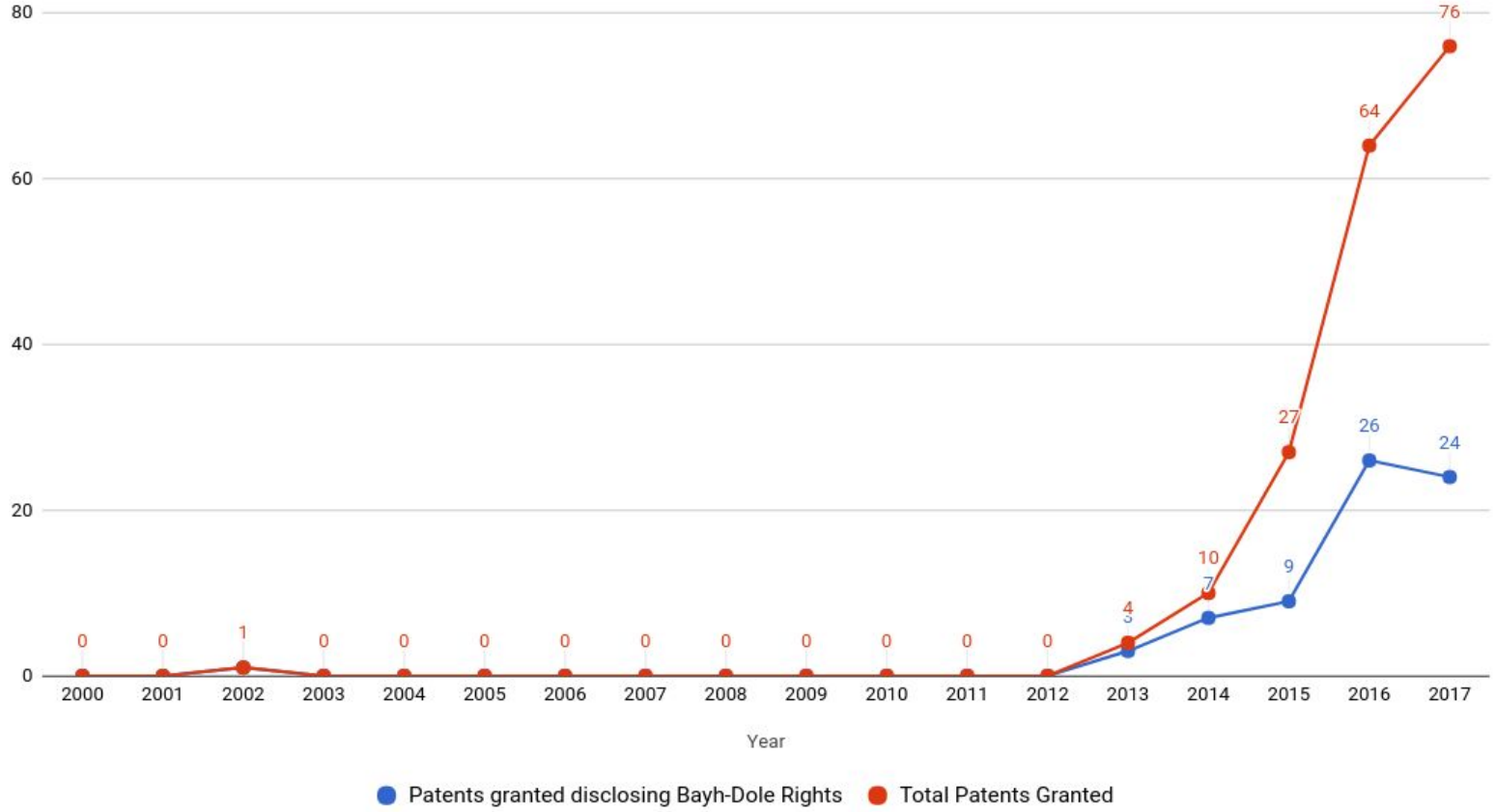


Through September 14, 2017

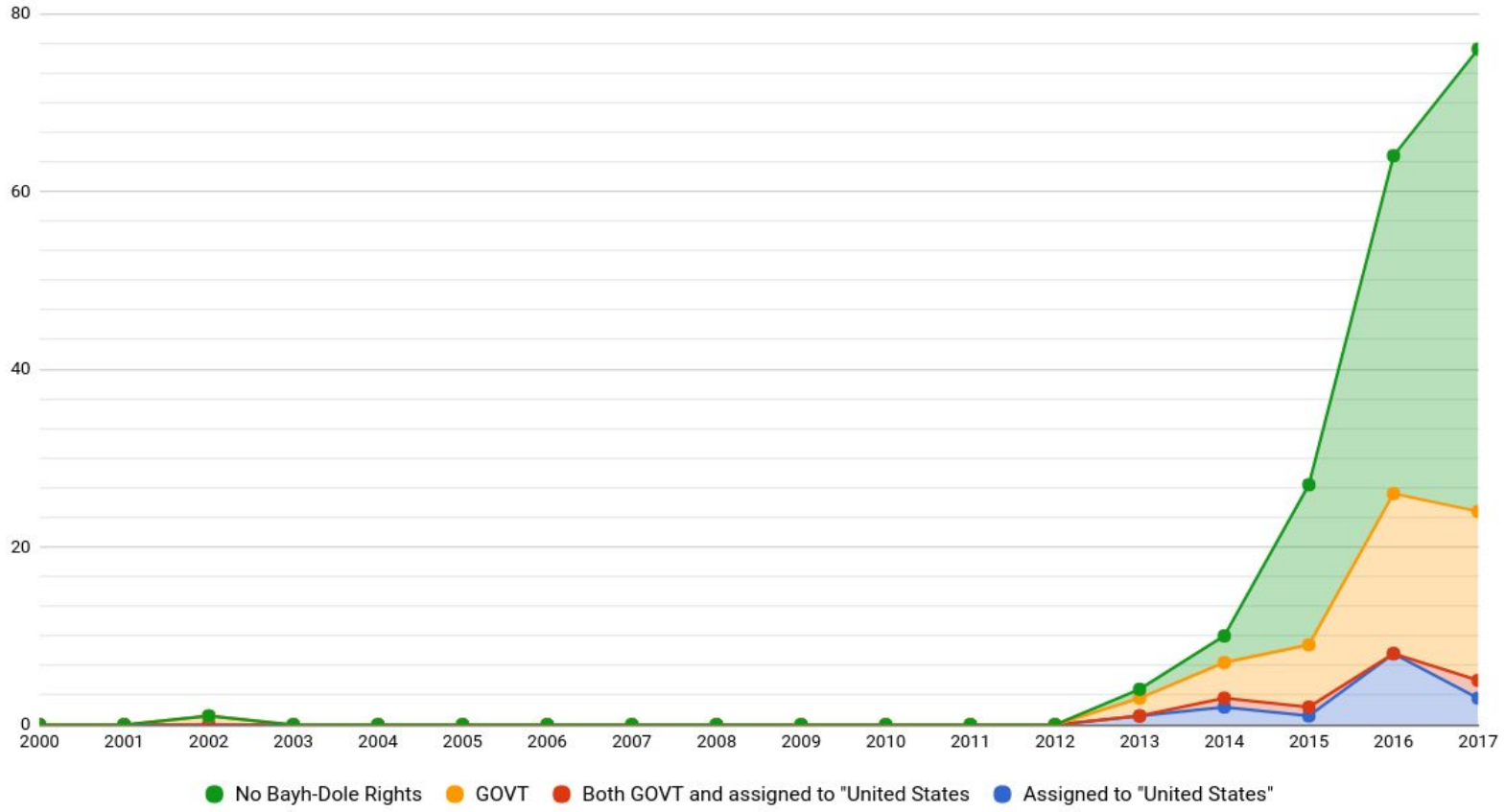
Year	Assigned to "United States"	GOVT	Both GOVT and "United States	Bayh-Dole Rights	No Bayh-Dole rights disclosed	Total
2002		1		1	0	1
2003				0	0	0
2004				0	0	0
2005				0	0	0
2006				0	0	0
2007				0	0	0
2008				0	0	0
2009				0	0	0
2010				0	0	0
2011				0	0	0
2012				0	0	0
2013	1	2	0	3	1	4
2014	2	4	1	7	3	10
2015	1	7	1	9	18	27
2016	8	18	0	26	38	64
2017	3	19	2	24	52	76

Patents issued by USPTO that mention “chimeric antigen receptor”

USPTO Patents Granted that mention "chimeric antigen receptor"



USPTO granted patents mentioning "chimeric antigen receptor"



NIH CAR T CRADAs

Here is a list of the NIH CAR T CRADAs entered into from 2010 to 2017.

Under reporting of CAR T patents

University of Pennsylvania patents (link here)

Fourteen CAR T patents assigned to UPenn have the same five inventors. Nine reported NIH funding, five did not.

	Patent Number	NIH Grants	Date filed	Earliest priority date	Carl H June	Michael D Kalos	Bruce L Levine	Michael C Milone	David L. Porter
2	9,499,629	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2012-06-14	2010-12-09	Y	Y	Y	Y	Y
3	8,906,682	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2013-07-10	2010-12-09	Y	Y	Y	Y	Y
4	8,911,993	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482	2013-07-10	2010-12-09	Y	Y	Y	Y	Y
5	9,328,156	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2013-12-16	2010-12-09	Y	Y	Y	Y	Y
6	8,916,381	None reported	2014-08-22	2010-12-09	Y	Y	Y	Y	Y
7	8,975,071	None reported	2014-08-22	2010-12-09	Y	Y	Y	Y	Y
8	9,102,760	None reported	2014-12-11	2010-12-09	Y	Y	Y	Y	Y
9	9,101,584	None reported	2014-12-12	2010-12-09	Y	Y	Y	Y	Y
10	9,102,761	None reported	2014-12-12	2010-12-09	Y	Y	Y	Y	Y
11	9,481,728	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2015-12-30	2010-12-09	Y	Y	Y	Y	Y
12	9,464,140	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2016-01-14	2010-12-09	Y	Y	Y	Y	Y
13	9,540,445	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2016-01-14	2010-12-09	Y	Y	Y	Y	Y
14	9,518,123	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2016-01-15	2010-12-09	Y	Y	Y	Y	Y
15	9,572,836	K24CA11787901, 1R01CA120409, 1R01CA105216, R01AI057838, R01113482** and 1PN2EY016586	2016-01-15	2012-07-13	Y	Y	Y		

What stuff costs

Apple iPhone X, $999

One year tuition and room and board at Stanford: $62,363

2017 Cadillac Escalade: $73,395, 2017 Tesla Model X: $79,500

Median annual cost of private room nursing home care in 2016: $92,378

Lamborghini’s Huracán: $203,295

Cost of new construction for 2,000 square foot home: $286,645

Kymriah: $475,000 (plus costs related to administration and care)

What exclusive rights are appropriate for CAR T

1. Much of early science was funded by governments, including in particular NIH.
2. There are complex and overlapping IPR claims, and litigation began early and is expected to expand.
3. There are patents that are asserted against multiple products, diseases and targets, and patents that will be asserted to limit entry to new products for particular diseases and treatment targets.
4. Exclusive rights have both positive and negative features. The positive feature is to induce investment in development of products with monopoly protection. The negative is to limit the approaches and products to address diseases and targets, rent seeking blocking patents and high transaction costs, and higher prices for products.
5. Super unlikely that the market will get the licensing right.

How should CAR T therapy be priced?

One can think of CAR T therapy as having three components:

1. Care (obtaining and **infusing** the **CAR T cells** back into the patient, monitoring and care during treatment, treatment for adverse effects).
2. Manufacturing the T cells.
3. Innovation.

The costs of manufacturing are not considered significant for high income countries. UPenn reported its costs of manufacturing were $15,000 and falling, five years ago.

The costs of care will be high, and higher in the United States than in countries that do a better job of controlling costs of hospitals and physicians.

The price for innovation is the most open question.

Context for setting prices for CAR T

1. The technology is new, with unknown but possibly very large health benefits for patients.
2. The costs of care will be high in the United States, and challenging in developing countries.
3. Investors are risk averse and expect high rates of returns.
4. Economies of scale are central to pricing innovation rewards/incentives. This cannot be overstated.
5. There is considerable uncertainty regarding the number of patients who will benefit from the treatment, in the United States and outside the United States.
6. Companies are investing billions of dollars acquire CAR T assets, in the expectation that prices will be unregulated.

Possible approach: Dynamic pricing

Monitor

- Require transparency of costs, by component, dynamically, to monitor changes in costs over time.
- Require transparency of revenues, profits from the delivery of the products.

Care

- Reimburse costs of care using traditional models.

Products

- Allow high prices for products **in the beginning**, to allow firms to have rapid recovery of risk adjusted R&D costs and to obtain robust rewards for successful advances in treatment outcomes.
- As companies reach **revenue/profit benchmarks**, begin to ratchet down prices.

Basic approach, have efficient sharing of risks between suppliers and payers, robust but reasonable rewards/incentives for innovation, and dynamic pricing, which trends down after benchmarks are met.

Patent pool for CAR T?

The federal government could use the leverage it has from the possible exercise of its Bayh-Dole rights or the use of 28 U.S.C. 1498(a) to induce patent holders to place the patents into a patent pool.

The royalties for the patent pool could be either:

1. Paid by product developers, or
2. Available royalty-free to developers, and paid by the federal government and or all third party payers, including the federal government.

CAR T patent pool

Benefits

- Greater freedom for product developers and manufacturers to innovation and compete.
- Lower prices.

Challenges

- Elimination of product monopolies reduces incentives to innovate.

Reformed incentives

- Create large innovation prize funds to reward innovation, including market entry/end product prizes.

Bayh-Dole Act issues

35 U.S.C. §201. Definitions

(f) The term “practical application” means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its **benefits are** to the extent permitted by law or Government regulations **available to the public on reasonable terms**. **[emphasis added]**

35 U.S.C. §202. Disposition of rights

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

(1) That the contractor disclose each subject invention to the Federal agency within a reasonable time after it becomes known to contractor personnel responsible for the administration of patent matters, and that **the Federal Government may receive title to any subject invention not disclosed to it within such time. [Emphasis added]**

35 U.S.C. §202. Disposition of rights

(c)(4) With respect to any invention in which the contractor elects rights, the Federal agency shall have a **nonexclusive, nontransferrable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world:** Provided, That the funding agreement may provide for such additional rights, including the right to assign or have assigned foreign patent rights in the subject invention, as are determined by the agency as necessary for meeting the obligations of the United States under any treaty, international agreement, arrangement of cooperation, memorandum of understanding, or similar arrangement, including military agreement relating to weapons development and production. [Emphasis added]

35 U.S.C. §202. Disposition of rights

(c) (5) The right of the Federal agency to require periodic reporting on the utilization or efforts at obtaining utilization that are being made by the contractor or his licensees or assignees: Provided, That any such information as well as any information on utilization or efforts at obtaining utilization obtained as part of a proceeding under section 203 of this chapter **shall be treated by the Federal agency as commercial and financial information obtained from a person and privileged and confidential and not subject to disclosure under section 552 of title 5. [Emphasis added]**

35 U.S.C. §202. Disposition of rights

(6) An obligation on the part of the contractor, in the event a United States patent application is filed by or on its behalf or by any assignee of the contractor, to include within the specification of such application and any patent issuing thereon, a statement specifying that the invention was made with Government support and that the Government has certain rights in the invention.

35 U.S.C. §202. Disposition of rights

(f)(1) No funding agreement with a small business firm or nonprofit organization shall contain a provision allowing a Federal agency to require the licensing to third parties of inventions owned by the contractor that are not subject inventions unless such provision has been approved by the head of the agency and a written justification has been signed by the head of the agency. Any such provision shall clearly state whether the licensing may be required in connection with the practice of a subject invention, a specifically identified work object, or both. The head of the agency may not delegate the authority to approve provisions or sign justifications required by this paragraph.

(2) A Federal agency shall not require the licensing of third parties under any such provision unless the head of the agency determines that the use of the invention by others is necessary for the practice of a subject invention or for the use of a work object of the funding agreement and that such action is necessary to achieve the practical application of the subject invention or work object. Any such determination shall be on the record after an opportunity for an agency hearing. Any action commenced for judicial review of such determination shall be brought within sixty days after notification of such determination.

35 U.S.C. §203. March-in rights

(a) . . .

(1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve **practical application** of the subject invention in such field of use;
(2) action is necessary to **alleviate health or safety needs which are not reasonably satisfied** by the contractor, assignee, or their licensees;
(3) action is necessary to meet **requirements for public use** specified by Federal regulations and such requirements are **not reasonably satisfied** by the contractor, assignee, or licensees; or

. . .

35 U.S.C. §203. March-in rights

(b) A determination pursuant to this section or section 202(b)(4) 1 shall not be subject to chapter 71 of title 41. An administrative appeals procedure shall be established by regulations promulgated in accordance with section 206. Additionally, any contractor, inventor, assignee, or exclusive licensee adversely affected by a determination under this section may, at any time within sixty days after the determination is issued, file a petition in the United States Court of Federal Claims, which shall have jurisdiction to determine the appeal on the record and to affirm, reverse, remand or modify, as appropriate, the determination of the Federal agency. In cases described in paragraphs (1) and (3) of subsection (a), **the agency's determination shall be held in abeyance pending the exhaustion of appeals or petitions filed under the preceding sentence. [Emphasis added]**

35 U.S.C. §209. Licensing federally owned inventions

(d) Terms and Conditions.—Any licenses granted under section 207(a)(2) shall contain such terms and conditions as the granting agency considers appropriate, and shall include provisions—

(1) retaining a nontransferrable, irrevocable, paid-up license for any Federal agency to practice the invention or have the invention practiced throughout the world by or on behalf of the Government of the United States;

35 U.S.C. §209. Licensing federally owned inventions

(d) (2) requiring periodic reporting on utilization of the invention, and utilization efforts, by the licensee, but only to the extent necessary to enable the Federal agency to determine whether the terms of the license are being complied with, except that any such report shall be treated by the Federal agency as commercial and financial information obtained from a person and privileged and confidential and not subject to disclosure under section 552 of title 5; and

35 U.S.C. §209. Licensing federally owned inventions

(3) empowering the Federal agency to **terminate** the license in whole or in part if the agency determines that—

(A) the licensee is not executing its commitment to achieve . . . **practical application** of the invention;

. . .

(C) termination is necessary to meet requirements for public use specified by Federal regulations issued after the date of the license, and such requirements are not reasonably satisfied by the licensee; **or**

(D) the licensee has been found by a court of competent jurisdiction to have violated the Federal antitrust laws in connection with its performance under the license agreement.