

Re: Prospective Grant of an Exclusive Patent License: Development and Commercialization of Engineered T Cell Therapies for the Treatment of HPV-Positive Cancer(s) to Scarlet TCR, Inc. (“Scarlet”), presently headquartered in Kingston, New Jersey.

FR Notice [88 FR 65179](#)

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Cc: Andy Burke, Lyric Jorgenson, Abby Rives

These comments from KEI concern the notice in the federal register regarding the prospective grant of an exclusive license to a company named Scarlet TCR. Inc., and KEI’s opposition to the grant of exclusive rights.

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### **Opposition to the exclusive license**

KEI Opposes the grant of an exclusive license to Scarlet on the grounds that the scope of exclusive rights is excessive and that the NIH should register the treatment with the FDA and provide non-exclusive licensing of the intellectual property rights in order to ensure that the technology is available and affordable.

The recent change in federal licensing regulations that eliminated the right of the public to obtain an administrative appeal of a licensing decision has created a situation where the public, based on little time or information, has one brief opportunity to challenge the creation of a legal monopoly on what is now a public asset.

The restrictions on the use of exclusive licensing of patented inventions in 35 USC 209(a) are designed to prevent cases like this, where an exclusive right in federally owned inventions is not a necessary incentive.

When the development of a product is already advanced, as is the case here, there is no basis to conclude that a worldwide, life-of-patent exclusive license is a “reasonable and necessary

incentive to call forth the investment capital and expenditures needed to bring the invention to practical application.” 35 USC 209(a)(1).

The public has well known concerns over the high costs of cancer treatments, and there is ample evidence that companies are charging extremely high prices for cell and gene therapies developed on federal grants.

The plethora of public statements of elected officials stating they want to do something about those costs is a stark contrast to this proposal by the NIH, to create an unneeded monopoly on an NIH developed and government owned cancer treatment.

As proposed, the license is a mechanism to privatize extensive public funding of both preclinical and clinical research to Scarlet, a company associated with the former NIH employee who led the NIH funded research effort.

Scarlet TCR is a small, mysterious entity without a web page that was registered in Delaware as a corporation February 17, 2023. Whoever owns that small company is basically positioning itself to resell the government’s patents, first to venture capitalists, and then to a larger company that actually has the means and resources to commercialize the technology.

The NIH has invented the treatment, manufactures the treatment itself, and funded and sponsored Phase I and Phase 2 clinical trials that will involve an estimated 180 patients.

As documented below, the FDA initial approval of similar cell therapies have generally relied on one or two trials with smaller enrollments than the trials the NIH is currently funding. Of the six cell therapies described below, five relied on smaller trials for approval.

All six cell therapies also qualified for Orphan Drug tax credits and Orphan Drug regulatory exclusivities, a type of protection from competition that exists without an exclusive patent license.

There is no case to argue that the NIH needs to grant worldwide life-of-patent exclusive licenses to get this treatment onto the market.

If the ongoing Phase II trial results are as good as the already concluded Phase I trial, the NIH can make its own application to the FDA for marketing approval. The NIH can subsequently license the technology to multiple private sector manufacturers on non exclusive licenses, saving US residents, including federal programs that provide health coverage, from paying a monopoly price on a government funded technology.

This is not a license for a pre-clinical technology. Scarlet TCR is a secretive start up company associated with a scientist who was recently employed by the NIH to work on the technology. While making former NCI employees extremely wealthy, even billionaires, may seem like a good cause at the NIH, it imposes huge fiscal costs on the rest of us.

## **The proposed licensed technology, field of use and licensed territory**

The Federal Register Notice includes five US patent applications filed from May 29, 2014 to August 1, 2022, and 27 foreign patents or applications.

From the Federal Register Notice:

The prospective exclusive license territory may be worldwide, and the field of use may be limited to the following:

“Development, manufacture and commercialization of autologous T cell therapy products that are genetically engineered to have stable expression of a T cell receptor (TCR) targeting human papillomavirus (“HPV”)–16 E7, as claimed in the Licensed Patent Rights, for the treatment of HPV-associated cancers and premalignant conditions in humans.”

The E–176–2014 patent family is primarily directed to an isolated TCR reactive to HPV 16 E7 antigen in the context of HLA–A\*02. HPV describes a group of human viruses known to cause malignancy. Of the group, HPV–16 is the most prevalent strain. Approximately 90% of adults are estimated to have been exposed at some point in their lifetime. HPV drives transformation of infected cells through the expression of certain oncoproteins, chiefly E5, E6 and E7. The latter two are constitutively expressed in malignant cells and are necessary to maintain a transformed state, rendering them useful therapeutic targets.

### **Scarlet TCR. Inc.**

There is little public information about this company. Scarlet TCR. Inc. has no web page. The company appeared to have been incorporated in Delaware on February 17, 2023. The NIH refused to provide information about the company to KEI.

### **Former NCI employee Dr. Christian Hinrichs.**

KEI assumes that Scarlet TCR was created by or at least has as a principal Dr. Christian Hinrichs, who currently is [employed](#) at the Rutgers Cancer Institute of New Jersey, where he is the Co-director the Duncan and Nancy MacMillan Cancer Immunology and Metabolism Center of Excellence.

Until recently, Hinrichs was a tenured Senior Investigator and Lasker Clinical Research Scholar at the National Cancer Institute (NCI). The NIH web page for Dr. Hinrichs describes his former role as “Senior Investigator and Chief of the Experimental Transplantation and Immunology Branch, National Cancer Institute-Center for Cancer Research.”

<https://www.nih.gov/research-training/lasker-clinical-research-scholars/tenured-former-scholars>

The NIH refused to confirm that Dr. Hinrichs was involved, but it seems likely, given his role working on the technology at the NCI or on NIH funded grants. Dr. Hinrichs claimed to have a relationship with Scarlet TCR in a [recent meeting](#) of cancer researchers. (Scarlet is also the name used for Rutgers sports teams and other projects).

Dr. Hinrichs seems to have a number of different industry positions since leaving the NCI. In a July 2023 meeting of the American Association for Cancer Research, Dr. Hinrichs also listed several industry relations. In addition to Scarlet TCR, Hinrichs mentioned PACT Pharma, Cargo Therapeutics, GlaxoSmithKline, Neogene Therapeutics and Capstan therapeutics.

KEI reached out to Dr. Hinrichs, asking if we could talk to him about Scarlet TCR and the exclusive license, but did not receive a response.

### **The stage of the technology**

Andy Burke informed KEI that the licensed technology is in the clinical stage, including the NIH funded Phase I/II trial [NCT02858310](#). ClinicalTrials.gov reports that this trial has an estimated enrollment of 180 patients, and a primary study complete date of December 12, 2025.

A Phase I/II Trial of T Cell Receptor Gene Therapy Targeting HPV-16 E7 for HPV-Associated Cancers

ClinicalTrials.gov ID NCT02858310

Sponsor: National Cancer Institute (NCI).

Principal Investigator: Scott M Norberg, D.O., National Cancer Institute (NCI).

Study Start (Actual) 2017-01-27

Primary Completion (Estimated) 2025-12-31

Study Completion (Estimated) 2026-01-01

Enrollment (Estimated) 180

Study Type Interventional

Human papillomavirus (HPV) can cause cervical, throat, anal, and genital cancers. Cancers caused by HPV have a HPV protein called E7 inside of their cells. In this new therapy, researchers take a person's blood, remove certain white blood cells, and insert genes that make them to target cancer cells that have the E7 protein. The genetically changed cells, called E7 TCR cells, are then given back to the person to fight the cancer. Researchers want to see if this can help people.

Andy Burke also helpfully called our attention to this paper published online February 2021 that reports on the Phase 1 part of the clinical trial:

Nagarsheth NB, Norberg SM, Sinkoe AL, Adhikary S, Meyer TJ, Lack JB, Warner AC, Schweitzer C, Doran SL, Korrapati S, Stevanović S, Trimble CL, Kanakry JA, Bagheri MH, Ferraro E, Astrow SH, Bot A, Faquin WC, Stroncek D, Gkitsas N, Highfill S, Hinrichs CS. TCR-engineered T cells targeting E7 for patients with metastatic HPV-associated epithelial cancers. *Nat Med.* 2021 Mar;27(3):419-425. doi: 10.1038/s41591-020-01225-1. Epub 2021 Feb 8. PMID: 33558725; PMCID: PMC9620481.  
<https://pubmed.ncbi.nlm.nih.gov/33558725/#full-view-affiliation-13>

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The paper provides acknowledgements, reports of competing interests and identifies relevant grants.

### **Acknowledgements**

This research was funded by the NIH Intramural Research Program and through a NIH Cooperative Research and Development Agreement with Kite, a Gilead Company

(C.S.H.). Support was also provided by the NHLBI-funded National Gene Vector Biorepository at Indiana University under contract no. 75N92019D00018 and by federal funding through the NCI, NIH, under contract no. 75N91019D00024 (C.S.H.). The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products or organizations imply endorsement by the US Government. The clinical-grade E7 TCR retroviral vector was manufactured by S. Feldman, NCI Surgery Branch.

### **Competing interests**

C.S.H. is an inventor on the NIH patent for the E7 TCR and other NIH patents in the field of immunotherapy. C.S.H. receives research funding through an NCI Collaborative Research and Development Agreement with Kite Pharma. The other authors declare no competing interests.

### **Grants and funding**

75N91019D00024/CA/NCI NIH HHS/United States  
75N92019D00018/HL/NHLBI NIH HHS/United States  
SI2 CA195682/CA/NCI NIH HHS/United States

### **The KITE CRADA**

Gilead has published a June 20, 2016 [press release](#) regarding its collaboration with the NIH on this technology.

Kite Pharma, Inc. (NASDAQ:KITE) today announced that it has entered into a new Cooperative Research and Development Agreement (CRADA) with the Experimental Transplantation and Immunology Branch (ETIB) of the National Cancer Institute (NCI) for the research and clinical development of T-cell receptor (TCR) product candidates directed against human papillomavirus (HPV)-16 E6 and E7 oncoproteins for the treatment of HPV-associated cancers.

Under the CRADA, NCI will evaluate a novel TCR therapy candidate targeting HPV-16 E7 as a monotherapy and in combination with a checkpoint inhibitor in HPV-16 associated solid tumors. This Phase 1/2 clinical study will be led by Christian S. Hinrichs, M.D., from the ETIB and lead investigator of this CRADA. The NCI will also continue to advance a separately designed TCR therapy candidate targeting HPV-16 E6, currently in a Phase 1/2 clinical trial, under an existing CRADA between Kite and the Surgery Branch of the NCI, led by Steven A. Rosenberg, M.D., Ph.D.

TCR therapies allow targeting of viral oncoproteins that are not effectively addressed with other existing therapeutic modalities. HPV-16 E6 and E7 TCR therapies hold the

potential to address the significant unmet medical need that exists in HPV-associated cancers," said Arie Belldegrun, M.D., FACS, Kite's Chairman, President, and Chief Executive Officer. "We are excited to collaborate with the network of talented investigators at the NCI as we advance our HPV-associated cancer therapy pipeline."

#### About HPV-Associated Cancers

Human papillomavirus (HPV) has a causal role in nearly all cervical cancers, and in many head and neck, and anogenital malignancies. HPV-16 is the most commonly found strain in these cancers. More than 33,000 cases of HPV-associated cancers are diagnosed each year in the US, and more than 11,000 annual deaths are attributed to the diseases, according to the Centers for Disease Control and Prevention. Current therapies for advanced HPV-associated tumors have low response rates and poor response duration.

### **Size of Trials in recent FDA Medical Reviews for Cell Therapies**

The trials the FDA relied upon for recent approvals of similar cell therapies are typically smaller than the NIH funded Phase I/II trial NCT02858310 associated with the Scarlet license. These are examples:

#### **BREYANZI** (lisocabtagene maraleucel, or JCAR017)

BLA STN: 125714

Approved June 24, 2022.

CD19-directed, genetically modified autologous T cell immunotherapy

Study JCAR017-BCM-003: 184 patients including 92 receiving JCAR017

Study 017006: 62 treated with JCAR017

Received 4 Orphan designations, and 3 Orphan approvals.

#### **CARVYKTI** (Ciltacabtagene autoleucel)

BLA STN: 125746/0

Approved February 2022.

B cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy

A single clinical trial provides the primary evidence of safety and efficacy for the BLA submission (ClinicalTrials.gov ID NCT03548207)

Actual Enrollment, 126

Orphan drug designed and approved for Treatment of multiple myeloma (MM)

#### **YESCARTA** (axicabtagene ciloleucel)

STN: BL 125643

CD19-directed genetically modified autologous T cell immunotherapy

Approved October 18, 2017

A single clinical trial provides the primary evidence of safety and effectiveness for the BLA submission, with an enrollment of 111.

Five Orphan designations and three orphan approvals

**TECARTUS:** (brexucabtagene autoleucel)

STN: BL 125703

CD19-directed genetically modified autologous T cell immunotherapy

Approval July 24, 2020

A single clinical trial, ZUMA-2, provides the primary evidence of safety and effectiveness for the BLA submission. 68 patients were treated with Tecartus

Three Orphan designations and two orphan approvals

**ABECMA** (idecabtagene vicleucel)

STN: BLA 125736

B cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy

Approved March 26, 2021

The safety and efficacy of Abecma were established in a multicenter study of 127 patients.

Orphan designation and approval for treatment of multiple myeloma

**KYMRIAH** (tisagenlecleucel)

STN: 125646

CD19-directed genetically modified autologous T cell immunotherapy

Approved August 2017

Approval of tisagenlecleucel was based on a single-arm trial of 63 patients.

Three orphan designations and three orphan approvals.

Priority Review Voucher issued

**Non patent regulatory barriers to entry**

The FDA regulatory pathway itself is a significant barrier to entry. The NIH should not provide exclusive rights to rely upon the NIH's trials for regulatory approval. If the NIH itself registers its own technology, the NIH can prevent third parties from claiming seven years of exclusivity under the Orphan Drug Act.

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October 6, 2023



## **ANNEX: Andy Burke Responses to KEI questions regarding the prospective license**

1. How does the worldwide geographic area reconcile with the PHS policy of promoting access in the developing countries? There is plenty of evidence that new cancer treatments are anything but accessible for the majority of the world's population.

**Response:** In general, a licensee may be granted a “worldwide” license even when (as is the case here) NIH’s patent coverage is much more limited. In countries where there are no patent rights, any party is free to utilize the technology.

2. What is the stage of the licensed technology?

**Response:** This technology is clinical stage.

3. Will the NIH have a cap on pricing relative to other high income countries (an international reference price cap)? And if not, why not?

**Response:** The terms of the license are subject to negotiation and have not been established at this point.

4. Is Christan Hinrichs involved in this license?

**Response:** I am unable to confirm one way or the other as this information is not public.

5. Hinrichs is a former NIH employee, who did work on these inventions at the NIH. Does he currently have grants for relevant work on the inventions since leaving the NIH?

**Response:** Please consider running a query through NIH RePORTER (<https://reporter.nih.gov/>) to identify relevant grant funding.

6. Has the NIH funded any clinical trials related to these inventions, at any time, and if so, what was the cost of the NIH funded or partially funded trials?

**Response:** I am aware of the Phase I/II study described in NCT02858310 (searchable on [clinicaltrials.gov](http://clinicaltrials.gov)). Initial results from the Phase I portion of this study have also published (please see PubMed ID 33558725).

7. Has the NIH made an estimate of the investments needed to bring the inventions to FDA approval, and if not, why not, given the restrictions on exclusive licenses in 35 USC 209?

**Response:** Consistent with 37 CFR 404.8(a)(8)(i), the applicant provides this estimate.

8. Has the NIH evaluated if a narrower geographic scope of exclusive rights would be appropriate for this license, for example, excluding countries with lower incomes or excluding the USA market?

Response: Consistent with 37 CFR 404.7, the determination that the scope of exclusivity is not “greater than reasonably necessary” can only be made after expiration of the public notice period. Please be aware that the public notice period for the contemplated license has not yet expired.