

## **Annex on costs of exercising the Crown Use Provisions as it relates to T-DM1**

In your response (Your Ref: TO-1061759 dated 23rd December 2016) to our submission you outlined the anticipated expense of over £1bn required to pursue a crown use licence.

“The Government has no plans to obtain the licenses/patents for products such as Kadcyla, as ministers believe that the potential costs involved in doing so and the considerable costs, which are over £1 billion, and risks associated with the development and manufacture of pharmaceutical products, should lie with the private pharmaceutical sector rather than with the Government, and hence taxpayers, or the NHS.”

It is unclear what this figure relates to, or over what time period, but we can address two issues, the compensation or royalty for the Crown Use License, and the costs of developing a biosimilar drug.

### **Compensation to patent holders**

The royalties the patent holders in this case are unlikely to be high, for several reasons

1. The key patents on T-DM1 are from ImmunoGen, by researchers who had been supported by the NIH to work on this issue, including but not limited to, from 1993 to 1999, five grants for which Ravi V. Chari was the principal investor, all dealing with either “Ideal drugs for anticancer conjugates” or “Drug Conjugate Therapy for Cancer Treatment.”
2. The T-DM1 patents are on the combination of two drugs that are now off patent: trastuzumab, a drug that entered the market in 1998 and which has already generated more than £50 billion for Roche, and DM1, a drug invented in the 1970s on a US NIH grant, and a widely available SMCC linker which is also off patent. While T-DM1 did represent an innovation as regards the use of an antibody-Drug Conjugate (ADC) to treat cancer, the fact that both drugs as well as the SMCC linker are all off patent, and the early research benefited from government funding, are favorable considerations in determining the value of the outstanding patents on T-DM1.
3. The global royalty payments from Roche to ImmunoGen on the T-DM1 patents are relatively small. The 2016 SEC 10-K report from ImmunoGen describes the Roche royalty payments for the licence to the T-DM1 patents as follows:

#### **UNITED STATES SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

**Form 10-K**

**For the transition period from July 1, 2016 to December 31, 2016 Commission file number 0-17999**

**ImmunoGen, Inc.**

#### **Roche**

In 2000, we granted Genentech, now a unit of Roche, an exclusive license to develop and commercialise HER2-targeting ADCs with our maytansinoid technology. Roche’s Kadcyla resulted from this license. Kadcyla was approved for marketing in the U.S., EU and Japan in 2013 based on the findings in the EMILIA Phase 3 trial. We received a \$2 million upfront payment from Roche upon execution of the agreement. We are entitled to receive up to a total of \$44 million in milestone payments, of which we have received \$34 million to date, and also tiered royalties on the commercial sales of Kadcyla or any other resulting products as described below.

In 2015, Immunity Royalty Holdings, L.P., or IRH, paid us \$200 million to purchase our right to receive 100% of the royalty payments on commercial sales of Kadcyla arising under our development and commercialization license with Genentech, until IRH has received aggregate Kadcyla royalties equal to \$235 million or \$260 million, depending on when the aggregate

Kadcyla royalties received by IRH reach a specified milestone. Once the applicable threshold is met, if ever, we will thereafter receive 85% and IRH will receive 15% of the Kadcyla royalties for the remaining royalty term.

The royalty term is determined on a country-by-country basis, and is initially 10 years from the date of first commercial sale of Kadcyla in the country. If, on such 10th anniversary, Kadcyla is covered by a valid claim under any patents controlled by us (excluding patents jointly owned by us and Genentech), then royalties remain payable on sales of Kadcyla in that country for an additional 2 years.

The royalty rate is based on the calendar-year sales of Kadcyla in two territories: (1) the U.S. and (2) the rest of the world. For each territory, the rate is: 3% of net sales up to \$250 million; 3.5% of net sales above \$250 million and up to \$400 million; 4% of net sales above \$400 million and up to \$700 million; and 5% of net sales above \$700 million in the that territory during the calendar year. Royalties will be reduced to a flat 2% of net sales in any country at any time during the royalty term in which Kadcyla is not covered by a valid claim under any patents controlled by us (excluding patents jointly owned by us and Genentech or solely owned by Genentech) in such country.

The license agreement also provides for certain adjustments to the royalties payable to us if Genentech makes certain third party license payments in order to exploit the ADC technology components of Kadcyla, although such adjustments would in no event reduce the royalties payable for any country below the greater of 50% of the royalties otherwise payable with respect to sales of Kadcyla in such country, or 2% of net sales in such country. As of the date of this report, we are unaware of any facts or circumstances that are reasonably likely to give rise to such an adjustment.

Roche may terminate this agreement for convenience at any time upon 90 days' prior written notice to us. The agreement may also be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the agreement will continue in effect until the expiration of Roche's royalty obligations.

Roche, through its Genentech unit, also has licenses for the exclusive right to use our maytansinoid ADC technology with antibodies to four undisclosed targets, which were granted under the terms of a separate, now expired 2000 right- to-test agreement with Genentech. For each of these licenses, we received a \$1 million license fee and are entitled to receive up to a total of \$38 million in milestone payments and also royalties on the sales of any resulting products. We have not received any milestone payments from these agreements through December 31, 2016. Roche is responsible for the development, manufacturing, and marketing of any products resulting from these licenses.

4. At present prices, the royalties from Roche to ImmunoGen represent approximately £3,000 pounds per patient, based upon a price of £102,000 per patient.
5. Roche has made investments in clinical trials to register this drug. These investments include Phase 1, 2 and 3 trials cited in the 2013 US FDA medical review of 1390 patients, which collectively are estimated to have cost less than £80 million. All of the Roche investments in clinical trials, including subsequent trials, benefit from more than a decade of intellectual property rights, separate from the patent protection, which give Roche exclusive rights to rely upon its clinical trials test data to register a drug. Roche can license or not license those data rights to biosimilar competitors, during the period of test data exclusivity. The remuneration for use of the patents does not have to fully compensate Roche for the costs of the trials, because the trials are protected by a separate form of intellectual property rights.
6. If the UK government uses its Crown Use authority to authorise competition for the supply of T-DM1, it will be doing so in order to remedy an abuse of the patent right, in this case, a remedy to Roche charging an excessive price. When governments use compulsory licences to remedy anticompetitive practices, the royalties are not designed to compensate

the patent holder from an infringement or loss. Royalties can be as low as zero, as a sanction, the standard used in the US Biologics Price Competition and Innovation act (BPCIA) when patent holders withhold certain patent landscape information from biosimilar competitors, or a reasonable royalty. The WTO TRIPS Agreement sets global standards for remuneration for Crown Use cases, and provides flexibility in cases where the non-voluntary authorization is to remedy an anti-competitive practice.

### **Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS)**

#### Article 31 - Other Use Without Authorization of the Right Holder

...

(h) the right holder shall be paid adequate remuneration in the circumstances of each case, taking into account the economic value of the authorization;

(k) Members are not obliged to apply the conditions set forth in subparagraphs (b) and (f) where such use is permitted to remedy a practice determined after judicial or administrative process to be anti-competitive. The need to correct anti-competitive practices may be taken into account in determining the amount of remuneration in such cases. . . .

### **Cost of biosimilar**

We have talked with experts and biosimilar companies who are confident that an affordable biosimilar product can reach the market, and issue explored in a December 2016 submission to the World Health Organization regarding the inclusion of T-DM1 on the WHO model list of essential medicines. In Table 12-1 of that submission is a list of 12 biosimilar and non-originator biologicals of trastuzumab approved or in development. DM1 is widely available today from generic suppliers at less than £2 for a three week treatment cycle, as a component of T-DM1. The SMCC linker is also available from generic suppliers, and it is inexpensive as well.

There will be costs associated with clinical trials for a biosimilar product, but here it is important to note that (1) the originator product was approved by the US FDA on the basis of trials involving 1390 patients, and (2) any biosimilar product will be sold in a number of markets outside of the UK. The UK government does not have to finance any of the costs of the biosimilar product, as it is not financing any of the biosimilar trials for trastuzumab or other drugs. That said, the UK could offer to finance or partly finance a biosimilar trial, in return for access to the approved drug at a deeply discounted price. This is an option, but not a requirement.

For these reasons and others, a Crown Use authorization will not present excessive or expensive outlays on royalties, and certainly, less in royalties than the current price of the drug, and the outlays on the royalties would only occur if a biosimilar product was on the market, at a cost saving price.

More to the point, and relevant to the patient situation today, as a practical matter, the mere threat to use the Crown Use authority is likely to radically change the dynamics of the negotiations over the T-DM1 price.

To your concern that pursuing this licence will weaken the future incentives for development of new medicines, the UK government is already pursuing alternative R&D models in the area of AMR. These models are applicable across all disease areas including cancer. These alternative innovation models will not force governments to choose between innovation or patients' access, but will facilitate both. Indeed, the WHO will consider a proposal at the World Health Assembly (WHA) meeting in May, to explore a new R&D fund for cancer that will enable governments to progressively delink R&D costs from drug prices.