GENENTECH TO PRESENT FIRST CLINICAL DATA ON NOVEL ANTI-TIGIT CANCER IMMUNOTHERAPY TIRAGOLUMAB AT ASCO

– Phase II CITYSCAPE trial shows promising results adding tiragolumab to Tecentriq in people with PD-L1-positive metastatic non-small cell lung cancer –

– Full results will be presented in an oral abstract session at the ASCO20 Virtual Scientific Program organized by the American Society of Clinical Oncology (ASCO) –

SOUTH SAN FRANCISCO, Calif. – May 13, 2020 – Genentech, a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), today announced positive results from the Phase II CITYSCAPE trial, the first randomized study evaluating the efficacy and safety of tiragolumab plus Tecentriq® (atezolizumab) compared with Tecentriq alone as an initial (first-line) treatment for people with PD-L1-positive metastatic non-small cell lung cancer (NSCLC). Tiragolumab is a novel cancer immunotherapy designed to bind to TIGIT, an immune checkpoint protein expressed on immune cells. Both TIGIT and PD-L1 play an important role in immune suppression, and blocking both pathways could enhance anti-tumor activity. The full results will be presented in an oral abstract session (Abstract #9503) at the ASCO20 Virtual Scientific Program organized by the American Society of Clinical Oncology (ASCO), which will be held May 29-31, 2020.

“We are pleased to share these first randomized anti-TIGIT results, showing that tiragolumab, our novel cancer immunotherapy, has encouraging efficacy and safety in combination with Tecentriq,” said Levi Garraway, M.D., Ph.D., chief medical officer and
head of Global Product Development. “TIGIT, an immune checkpoint protein expressed on immune cells, was identified by our own scientists. By blocking both TIGIT and PD-L1 pathways simultaneously, we hope to deepen patient responses to immunotherapy and widen the circle of people who may benefit.”

At the primary analysis, tiragolumab plus Tecentriq met both co-primary endpoints in the intention-to-treat (ITT) population, showing an improvement in the objective response rate (ORR) (31.3% versus 16.2%) and a 43% reduction in the risk of disease worsening or death (progression-free survival; PFS) (median PFS=5.4 versus 3.6 months; hazard ratio [HR] = 0.57, 95% CI: 0.37–0.90) compared with Tecentriq alone.

An exploratory analysis in people with high levels of PD-L1 (TPS ≥50%) showed a clinically meaningful improvement in ORR (55.2% versus 17.2%) and a 67% reduction in the risk of disease worsening or death (median PFS=not reached versus 3.9 months; HR=0.33, 95% CI: 0.15–0.72) with the combination compared with Tecentriq alone.

The data suggest that the combination of tiragolumab plus Tecentriq was well-tolerated, showing similar rates of all Grade 3 or more all-cause adverse events (AEs) when combining the two immunotherapies compared with Tecentriq alone (41.8% versus 44.1%).

At a six-month follow-up, the improvement in the ORR and PFS in the tiragolumab plus Tecentriq arm persisted in both the ITT and the PD-L1-high populations, and no new safety signals were observed.

As part of Genentech’s commitment to explore new immunotherapy options and combinations, the company recently initiated two Phase III clinical trials evaluating tiragolumab plus Tecentriq for people with certain types of lung cancer (SKYSCRAPER-01 and SKYSCRAPER-02). Tiragolumab is also being evaluated in other solid tumors as well as in hematological cancers. Additional Phase Ia/b results in
solid tumors will be presented at an upcoming medical meeting.

**About CITYSCAPE study**

CITYSCAPE is a global Phase II, randomized and blinded study evaluating tiragolumab plus Tecentriq compared with Tecentriq alone in 135 patients with first-line PD-L1-positive, locally advanced unresectable or metastatic non-small cell lung cancer. Patients were randomized 1:1 to receive either tiragolumab plus Tecentriq or placebo plus Tecentriq, until progressive disease or loss of clinical benefit. Co-primary endpoints are objective response rate (ORR) and progression free survival (PFS). Secondary endpoints include safety and overall survival (OS).

**Efficacy results**

<table>
<thead>
<tr>
<th></th>
<th>ITT (TPS ≥1%) N=135</th>
<th>PD-L1-high (TPS ≥50%) N=58</th>
<th>PD-L1-low (TPS 1-49%) N=77</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tiragolumab + Tecentriq (n=67)</td>
<td>31.3 (19.5, 43.2)</td>
<td>55.2 (35.3, 75.0)</td>
<td>13.2 (1.15, 25.2)</td>
</tr>
<tr>
<td>placebo + Tecentriq (n=68)</td>
<td>16.2 (6.7, 25.7)</td>
<td>17.2 (1.8, 32.7)</td>
<td>15.4 (2.8, 28.0)</td>
</tr>
<tr>
<td><strong>ORR, % (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Odds ratio (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tiragolumab + Tecentriq (n=29)</td>
<td>2.57 (1.07, 6.14)*</td>
<td>5.91 (1.76, 19.81)*</td>
<td>0.83 (0.23, 3.00)*</td>
</tr>
<tr>
<td>placebo + Tecentriq (n=29)</td>
<td>16.2 (6.7, 25.7)</td>
<td>17.2 (1.8, 32.7)</td>
<td>15.4 (2.8, 28.0)</td>
</tr>
<tr>
<td><strong>Median PFS (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tiragolumab + Tecentriq (n=38)</td>
<td>5.4 (4.2, NE)</td>
<td>3.9 (2.1, 4.7)</td>
<td>4.1 (1.6, 5.6)</td>
</tr>
<tr>
<td>placebo + Tecentriq (n=39)</td>
<td>3.6 (2.7, 4.4)</td>
<td>3.9 (2.1, 4.7)</td>
<td>3.6 (1.5, 5.0)</td>
</tr>
<tr>
<td><strong>HR (95% CI)</strong></td>
<td>0.57 (0.37, 0.90)*</td>
<td>0.33 (0.15, 0.72)*</td>
<td>0.85 (0.49, 1.48)*</td>
</tr>
</tbody>
</table>

At a six-month follow-up, the improvement in ORR (37.3% versus 20.6%) and PFS (median PFS=5.6 months versus 3.9 months) in the tiragolumab plus Tecentriq arm persisted in the ITT population. Results in the PD-L1-high population were also consistent with the first analysis and the median PFS was still not reached.
### Safety results

<table>
<thead>
<tr>
<th></th>
<th>tiragolumab + Tecentriq n=67</th>
<th>placebo + Tecentriq n= 68</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grade 3-5 AEs</td>
<td>41.8%</td>
<td>44.1%</td>
</tr>
<tr>
<td>Treatment-related AEs (TRAEs)</td>
<td>80.6%</td>
<td>72%</td>
</tr>
<tr>
<td>Grade ≥3 TRAEs</td>
<td>14.9%</td>
<td>19.1%</td>
</tr>
<tr>
<td>AEs leading to treatment withdrawal</td>
<td>7.5%</td>
<td>10.3%</td>
</tr>
</tbody>
</table>

### About tiragolumab
Tiragolumab is a monoclonal antibody designed to bind with TIGIT, a protein receptor on immune cells. By binding to TIGIT, tiragolumab blocks its interaction with a protein called poliovirus receptor (PVR, or CD155) that can suppress the body's immune response. Blockade of TIGIT and PD-L1 may synergistically enable the re-activation of T cells and enhance NK cell antitumor activity.

### About Tecentriq® (atezolizumab)
Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1. Tecentriq is designed to bind to PD-L1 expressed on tumor cells and tumor-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, Tecentriq may enable the re-activation of T cells. Tecentriq may also affect normal cells.

### Tecentriq U.S. Indications
Tecentriq is a prescription medicine used to treat adults with:

**A type of bladder and urinary tract cancer called urothelial carcinoma.** Tecentriq may be used when your bladder cancer:
● has spread or cannot be removed by surgery, **and if you have any one of the following conditions:**
  ○ you are not able to take chemotherapy that contains a medicine called cisplatin, and your cancer tests positive for “PD-L1”, or
  ○ you are not able to take chemotherapy that contains any platinum regardless of “PD-L1” status, or
  ○ you have tried chemotherapy that contains platinum, and it did not work or is no longer working.

The approval of Tecentriq in these patients is based on a study that measured response rate and duration of response. Continued approval for this use may depend on the results of an ongoing study to confirm benefit.

**A type of lung cancer called non-small cell lung cancer (NSCLC).**

● Tecentriq may be used with chemotherapy and other anti-cancer medicines as your first treatment when your lung cancer:
  ○ has spread or grown, **and**
  ○ is a type called “non-squamous NSCLC”, **and**
  ○ your tumor does not have an abnormal “EGFR” or “ALK” gene.

● Tecentriq may be used alone when your lung cancer:
  ○ has spread or grown, **and**
  ○ you have tried chemotherapy that contains platinum, and it did not work or is no longer working.
  ○ If your tumor has an abnormal “EGFR” or “ALK” gene, you should have also tried an FDA-approved therapy for tumors with these abnormal genes, and it did not work or is no longer working.

**A type of breast cancer called triple-negative breast cancer (TNBC).**

Tecentriq may be used with the medicine paclitaxel protein-bound when your breast cancer:
○ has spread or cannot be removed by surgery, and
○ your cancer tests positive for “PD-L1.”

The approval of Tecentriq in these patients is based on a study that measured the amount of time until patients’ disease worsened. Continued approval for this use may depend on results of an ongoing study to confirm benefit.

A type of lung cancer called small cell lung cancer (SCLC).

● Tecentriq may be used with the chemotherapy medicines carboplatin and etoposide as your first treatment when your lung cancer:
  ○ is a type called “extensive-stage small cell lung cancer,” which means that it has spread or grown.

It is not known if Tecentriq is safe and effective in children.

Important Safety Information

What is the most important information about Tecentriq?

Tecentriq can cause the immune system to attack normal organs and tissues and can affect the way they work. These problems can sometimes become serious or life threatening and can lead to death.

Patients should call or see their healthcare provider right away if they get any symptoms of the following problems or these symptoms get worse.

Tecentriq can cause serious side effects, including:

● Lung problems (pneumonitis)—signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain
● Liver problems (hepatitis)—signs and symptoms of hepatitis may include yellowing of the skin or the whites of the eyes, severe nausea or vomiting, pain on the right side of the stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual
● **Intestinal problems (colitis)**—signs and symptoms of colitis may include diarrhea (loose stools) or more bowel movements than usual, blood or mucus in stools or dark, tarry, sticky stools, and severe stomach area (abdomen) pain or tenderness

● **Hormone gland problems (especially the thyroid, adrenal glands, pancreas, and pituitary)**—signs and symptoms that the hormone glands are not working properly may include headaches that will not go away or unusual headaches, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, changes in mood or behavior (such as decreased sex drive, irritability, or forgetfulness), feeling cold, constipation, the voice gets deeper, urinating more often than usual, nausea or vomiting, and stomach area (abdomen) pain

● **Problems in other organs**—signs and symptoms may include severe muscle weakness, numbness or tingling in hands or feet, confusion, blurry vision, double vision, or other vision problems, changes in mood or behavior, extreme sensitivity to light, neck stiffness, eye pain or redness, skin blisters or peeling, chest pain, irregular heartbeat, shortness of breath, or swelling of the ankles

● **Severe infections**—signs and symptoms of infection may include fever, cough, flu-like symptoms, pain when urinating, and frequent urination or back pain

● **Severe infusion reactions**—signs and symptoms of infusion reactions may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, swelling of your face or lips, dizziness, fever, feeling like passing out, and back or neck pain

**Getting medical treatment right away may help keep these problems from becoming more serious.** A healthcare provider may treat patients with corticosteroid or hormone replacement medicines. A healthcare provider may delay or completely stop treatment with Tecentriq if patients have severe side effects.
Before receiving Tecentriq, patients should tell their healthcare provider about all of their medical conditions, including if they:

- have immune system problems (such as Crohn’s disease, ulcerative colitis, or lupus); have had an organ transplant; have lung or breathing problems; have liver problems; have a condition that affects the nervous system (such as myasthenia gravis or Guillain-Barre syndrome); or are being treated for an infection

- are pregnant or plan to become pregnant. Tecentriq can harm an unborn baby. Patients should tell their healthcare provider right away if they become pregnant or think they may be pregnant during treatment with Tecentriq. **Females who are able to become pregnant:**
  - a healthcare provider should do a pregnancy test before they start treatment with Tecentriq
  - they should use an effective method of birth control during their treatment and for at least 5 months after the last dose of Tecentriq
- are breastfeeding or plan to breastfeed. It is not known if Tecentriq passes into the breast milk. Patients should not breastfeed during treatment and for at least 5 months after the last dose of Tecentriq

**Patients should tell their healthcare provider about all the medicines they take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**The most common side effects of Tecentriq when used alone include:**

- feeling tired or weak
- nausea
- cough
- shortness of breath
The most common side effects of Tecentriq when used in lung cancer with other anti-cancer medicines include:

- feeling tired or weak
- nausea
- hair loss
- constipation
- diarrhea
- decreased appetite

The most common side effects of Tecentriq when used in triple-negative breast cancer with paclitaxel protein-bound include:

- hair loss
- tingling or numbness in hands or feet
- feeling tired
- nausea
- diarrhea
- low red blood cells (anemia)
- constipation
- cough
- headache
- low white blood cells
- vomiting
- decreased appetite

Tecentriq may cause fertility problems in females, which may affect the ability to have children. Patients should talk to their healthcare provider if they have concerns about fertility.
These are not all the possible side effects of Tecentriq. Patients should ask their healthcare provider or pharmacist for more information about the benefits and side effects of Tecentriq.

Report side effects to the FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch. Report side effects to Genentech at 1-888-835-2555.

Please visit http://www.Tecentriq.com for the Tecentriq full Prescribing Information for additional Important Safety Information.

About Genentech in cancer immunotherapy

Genentech has been developing medicines to redefine treatment in oncology for more than 35 years, and today, realizing the full potential of cancer immunotherapy is a major area of focus. With more than 20 immunotherapy molecules in development, Genentech is investigating the potential benefits of immunotherapy alone, and in combination with various chemotherapies, targeted therapies and other immunotherapies with the goal of providing each person with a treatment tailored to harness their own unique immune system.

In addition to Genentech’s approved PD-L1 checkpoint inhibitor, the company’s broad cancer immunotherapy pipeline includes other checkpoint inhibitors, individualized neoantigen therapies and T cell bispecific antibodies. For more information visit http://www.gene.com/cancer-immunotherapy.

About Genentech in lung cancer

Lung cancer is a major area of focus and investment for Genentech, and we are committed to developing new approaches, medicines and tests that can help people with this deadly disease. Our goal is to provide an effective treatment option for every person diagnosed with lung cancer. We currently have five approved medicines to treat certain kinds of lung cancer and more than 10 medicines being developed to target the
most common genetic drivers of lung cancer or to boost the immune system to combat the disease.

**About Genentech**

Founded more than 40 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with serious and life-threatening medical conditions. The company, a member of the Roche Group, has headquarters in South San Francisco, California. For additional information about the company, please visit [http://www.gene.com](http://www.gene.com).

###