Media Release

Roche to present new and updated data at ESMO 2019 reinforcing the use of Alecensa in the first-line setting for advanced ALK-positive non-small cell lung cancer

- **New real-world data from the Flatiron database supports clinical benefits of Alecensa® (alectinib) across time to treatment discontinuation, real-world progression free survival and overall survival**
- **Final PFS and updated data from the pivotal Phase III ALEX study reinforces efficacy of Alecensa in first-line ALK-positive non-small cell lung cancer and shows progression free survival of nearly three years**

Basel, 28 September 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will present new data at the European Society for Medical Oncology (ESMO) 2019 congress, announcing the results of a number of studies in patients receiving Alecensa® (alectinib) for anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).

"The data presented at ESMO this year further demonstrate the well-established benefits of Alecensa, and confirm its use as the standard of care for newly diagnosed advanced or metastatic ALK-positive lung cancer patients," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "The positive results from our real-world data study further support the benefits we have seen from our Phase III clinical studies."

Real-world data results in patients with ALK-positive NSCLC
Insights utilising real-world data from the Flatiron Health database will be presented at the congress on Saturday 28 September (Abstract #1546P, 12:00 CEST). These data further support the benefits of Alecensa in the real-world setting, where real-world progression free survival (rwPFS), time to treatment discontinuation (TTD - used as a surrogate for real-world treatment duration) and overall survival (OS) were demonstrated to be longest in Alecensa treated patients with previously untreated ALK-positive NSCLC. The results also show that despite the established benefit of individual ALK inhibitors (ALKi) as first-line therapies and the inclusion of ALKi in many clinical guidelines, as recently as 2017 and 2018 more than 25% of patients with ALK-positive NSCLC received a non-ALKi as first-line therapy. Data were available for 620 patients with ALK-positive advanced NSCLC.

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Group Communications Roche Group Media Relations
Tel. +41 61 688 88 88 www.roche.com

1L	Outcome	Statistics	Alectinib (n=98)	Ceritinib (n=4)	Crizotinib (n=318)	non-ALKi (n=200)
	rwPFS	Median (95% CI), months	NR	5.06 (0.72, NR)	6.41 (5.92, 8.16)	8.26 (6.25, 9.9)
		6-month probability (95% CI)	0.83 (0.75, 0.91)	0.5 (0.19, 1)	0.55 (0.49, 0.6)	0.59 (0.52, 0.66)
		12-month probability (95% CI)	0.68 (0.58, 0.79)	0.25 (0.05, 1)	0.32 (0.27, 0.38)	0.37 (0.3, 0.44)
	TTD	Median (95% CI), months	NR	6.1 (0.72, NR)	7.57 (6.97, 9.14)	3.12 (2.76, 4.38)
		6-month probability (95% CI)	0.85 (0.78, 0.92)	0.5 (0.19, 1)	0.61 (0.56, 0.67)	0.35 (0.29, 0.43)
		12-month probability (95% CI)	0.73 (0.64, 0.84)	0.25 (0.05, 1)	0.36 (0.31, 0.42)	0.21 (0.16, 0.28)
	OS	Median (95% CI), months	NR	6.1 (0.72, NR)	23.06 (16.51, 30.86)	27.99 (21.6, 36.51)
		6-month probability (95% CI)	0.92 (0.87, 0.98)	0.5 (0.19, 1)	0.78 (0.73, 0.82)	0.84 (0.79, 0.89)
		12-month probability (95% CI)	0.85 (0.77, 0.93)	0.25 (0.05, 1)	0.65 (0.6, 0.7)	0.71 (0.65, 0.78)

1L, first-line therapy; ALKi, ALK inhibitor; rwPFS, real-world progression-free survival; TTD, time to treatment discontinuation; OS, overall survival; NR, not reached (median survival estimate could not be calculated). 6 & 12-month probability is the event-free survival probability for the following events: progression, treatment discontinuation and death at 6 months and at 12 months, respectively.

Final PFS and updated Phase III ALEX data

Final PFS and updated results from the pivotal Phase III ALEX study, to be presented on Sunday 29 September during a poster discussion (Abstract #1484PD, 16:30 CEST), confirm the superior efficacy and tolerability of Alecensa in comparison to crizotinib in patients with untreated ALK-positive NSCLC, reducing the risk of disease worsening or death by 57% (hazard ratio [HR]=0.43, 95% CI: 0.32–0.58). Mature data show that Alecensa provides a median investigator-assessed progression free survival (PFS) of nearly three years (34.8 months, 95% CI: 17.7-not reached [NR]) versus 10.9 months (95% CI: 9.1–12.9) in those who received crizotinib.

Alecensa also demonstrated superior efficacy compared to crizotinib regardless of the presence of central nervous system (CNS) metastases at baseline. For those with CNS metastases, the median investigator-assessed PFS was 25.4 months for Alecensa versus 7.4 months for crizotinib (HR=0.37, 95% CI: 0.23–0.58). In

those without CNS metastases, it was 38.6 months versus 14.8 months respectively (HR=0.46, 95% CI: 0.31–0.68). Despite longer median treatment duration with Alecensa versus crizotinib (27.7 months versus 10.8 months), the safety profile for Alecensa remains favourable; fewer Alecensa-treated patients experienced Grade 3–5 adverse events (AEs) (48.7% versus 55.0% crizotinib).

BFAST

On Monday 30 September (08:30 - 10:00 CEST, Abstract LBA81), Roche will also present results from the first cohort of the Phase II/III Blood First Assay Screening Trial (BFAST). BFAST is the first prospective trial to use blood-based next generation sequencing (NGS) as the sole method of identifying and assigning NSCLC patients to targeted therapy based on actionable genetic alterations without the need for tissue biopsy. The study utilised FoundationOne® Liquid, Foundation Medicine's liquid (blood) biopsy assay to detect fusions in circulating tumour DNA (ctDNA) from a simple blood draw to identify ALK status and consequently eligibility for Alecensa.

About the ALEX Study

ALEX (NCT02075840/B028984) is a randomised, multicentre, open-label, Phase III study evaluating the efficacy and safety of Alecensa versus crizotinib in treatment-naïve patients with ALK-positive NSCLC whose tumours were characterised as ALK-positive by the VENTANA ALK (D5F3) CDx Assay, a companion immunohistochemistry (IHC) test developed by Roche Tissue Diagnostics. Patients were randomised (1:1) to receive either Alecensa or crizotinib. The primary endpoint of the ALEX study was PFS as assessed by the investigator, and secondary endpoints include: Independent Review Committee (IRC)-assessed PFS, time to CNS progression, objective response rate (ORR), duration of response (DOR) and OS. The multicentre study was conducted in 303 people across 161 sites in 31 countries. OS data continue to be considered immature.

About the real-world data Study

The real-world data study is a retrospective cohort study that utilised US electronic health record data from Flatiron Health, a nationwide database containing de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction. Treatment patterns and outcomes, including real-world progression free survival (rwPFS) and overall survival (OS) were extracted for first- or second-line therapy. Time to treatment discontinuation (TTD) was used as a surrogate for real-world treatment duration accounting for treatment beyond progression. Time-to-event analyses were performed using Kaplan-Meier methods. Patients included were diagnosed with stage IIIB-IV ALK-positive NSCLC between 01 January 2011 and 30 September 2018. Data were available for 620 patients with ALK-positive advanced NSCLC. An ALKi was given to 420/620 (67.7%) patients as first-line therapy.

About Alecensa

Alecensa (RG7853/AF-802/RO5424802/CH5424802) is a highly selective, CNS active, oral medicine created at Chugai Kamakura Research Laboratories and is being developed for people with NSCLC whose tumours are identified as ALK-positive. ALK-positive NSCLC is often found in younger people who have a light or non-smoking history. It is almost always found in people with a specific type of NSCLC called adenocarcinoma. Alecensa is now approved in 83 countries as an initial (first-line) treatment for ALK-positive, metastatic NSCLC, including in the US, Europe, Japan and China.

About Roche in lung cancer
Lung cancer is a major area of focus and investment for Roche, 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 ten medicines being developed to target the most common genetic drivers of lung cancer or to boost the immune system to combat the disease.

About Roche
Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the eleventh consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: media.relations@roche.com
- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein