Media Release

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Roche committed to innovation and growth

Personalised healthcare leadership and world-class pipeline presented at investor conference

- **Industry-leading pipeline with 72 new molecular entities (NMEs); 19 late-stage clinical trials, 12 of which involve NMEs, expected to read out over the next 18 months**
- **Personalised healthcare solutions progressing well by leveraging capabilities across Pharma and Diagnostics: more than 200 companion diagnostic projects within the Group**
- **Antibody–drug conjugates and synergistic combinations highlighted as two of the most promising new cancer technologies; a number of early-stage clinical candidates in addition to T–DM1 and Perjeta/Herceptin currently in development**
- **Pipeline in metabolism and neuroscience progressing well with aleglitazar confirming renal safety profile in AleNephro study and gantenerumab's Alzheimer's programme expanded**
- **Tailor-made options to increase access to Roche's medicines in emerging markets**
- **Commitment to stable R&D budget, striving for efficiency and sustainable cash flow**

Roche (SIX: RO, ROG; OTCQX: RHHBY) will today give an update on its strategy, which continues to be focused on medical innovation and sustainable growth. Through its leadership in personalised healthcare, Roche is uniquely positioned to develop therapies that advance current standards of care and improve people's lives. Innovative access strategies in developed and emerging markets will provide additional growth opportunities. The investor event in London will showcase the progress of Roche's late-stage pipeline. As many as 19 late stage clinical trials are expected to read out over the next 18 months, 12 of which are investigating new molecular entities (NMEs). In addition, three NME projects could reach the Lifecycle Investment Point (LIP) to move into late-stage development this year. Despite the promising increase of late–stage projects, Roche intends to keep its R&D budget stable by implementing continued productivity improvements and rigorous portfolio prioritisation.

"Roche's strategy is based on developing differentiated medicines and diagnostics in areas of high unmet need that bring true medical benefit to patients," said Severin Schwan, CEO of Roche. "More than 60% of our pharmaceutical pipeline projects are coupled with the development of companion diagnostics in order to

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make treatments more effective. The recent launches of our cancer medicines Perjeta and Zelboraf are examples of the concept of personalised healthcare becoming reality."

Roche is working to improve patient access in developed countries, as well as in emerging markets, where increasing income levels and the development of public healthcare are driving the demand to prescribe and administer highly innovative medicines. Roche's broad portfolio allows for flexible commercial schemes and value-based pricing. In emerging markets, access programmes implemented over the last few years have helped significantly increase the number of people who can be treated with Roche medicines.

Diagnostics: sustained growth and strengthened leadership through innovation

Roche Diagnostics continues to improve testing efficiency at labs around the world through its unique and complete menu offering that includes high-value assays and enhanced platforms. Roche is leading the discovery of new biomarkers supported by clinical evidence, in collaboration with Roche Pharma and also third parties. By successfully tailoring its strategy to local conditions in different emerging markets, Roche Diagnostics has been expanding its commercial reach, continuing its double-digit sales growth and its leadership in these vibrant markets.

Oncology: a broad set of technologies for targeted therapies

One of Roche's core competencies is oncology, and about 50% of our R&D budget is allocated to this franchise. Over the next few years, new technologies are expected to expand the current product portfolio for patients suffering from cancer.

Antibody–drug conjugates: Roche is at the forefront in developing antibody–drug conjugates (ADCs) that combine the specificity of antibodies with the power of chemotherapy and may result in improved efficacy and fewer adverse events. **T–DM1** is an investigational ADC that attaches trastuzumab to the chemotherapy agent DM1 via a stable linker. It is designed to target and inhibit HER2 signalling and deliver the chemotherapy directly inside HER2-positive cancer cells. Pivotal phase III data for T–DM1 showed significant and clinically meaningful improvements in progression-free and overall survival in pretreated patients with advanced HER2-positive breast cancer compared with lapatinib plus Xeloda chemotherapy. The data were submitted for approval to global health authorities in August 2012 and updated overall survival data will be presented at an upcoming medical meeting. T–DM1 will be used in patients identified with a HER2 companion diagnostic test.

Roche has a total of nine ADCs in its development pipeline. Today, preliminary data for **RG7593**, a humanised IgG1 **anti-CD22** monoclonal antibody (anti-CD22) conjugated to an anti-mitotic agent, will be presented. RG7593 is currently being tested in phase I in haematological cancers. The data indicate very promising anti-tumour activity in patients with relapsed or refractory disease following treatment with anti-CD20 containing therapies.

Synergistic combinations: Roche is the leader in the development of therapy combinations that have the potential to overcome resistance by targeting multiple pathways in cancer. Synergistic combinations also offer the potential for improved efficacy. A prominent example is recently approved **Perjeta** in combination with Herceptin and chemotherapy, which has the potential to become the new standard of care in the frontline treatment of HER2-positive metastatic breast cancer. The mechanisms of action of Perjeta (pertuzumab) and Herceptin (trastuzumab) complement each other and enable a more comprehensive blockade of the HER signalling pathway. Perjeta will be used in connection with a HER2 companion diagnostics test.

- **Onartuzumab (MetMAb),** a unique monovalent antibody, is being studied in combination with Tarceva in patients whose tumours overexpress MET in METLUNG, a phase III study in second/third line non-small cell lung cancer (NSCLC). Results from METLUNG are expected in 2014. Onartuzumab is also being studied in combination with a paclitaxel regimen with or without Avastin in several further cancer types, such as breast and colon. New phase II studies in squamous and non-squamous non-small cell lung cancer, as well as in gastric cancer and glioblastoma began enrolment in 2012. A companion diagnostic test to identify people with MET-positive tumours is in development.

- Promising early preclinical data showed that combining anti-VEGF with **anti-EGFL7** reduced tumour vascular function and inhibited tumour growth in advanced solid tumours. **RG7414** is a humanised antibody against EGFL7 (epidermal growth factor domain-like 7), and is currently being studied in combination with Avastin in phase II trials in lung and colorectal cancer. The combination may improve anti-angiogenic treatment and potentially lead to a new role for Avastin in treating a range of cancers.

- **RG7601**, a novel small molecule **Bcl-2 selective inhibitor** currently being studied in phase I in haematological cancers, is designed to restore apoptosis, also known as programmed cell death. Bcl-2 family proteins are expressed at high levels in many tumours. Inhibiting Bcl-2 may restore apoptosis and, consequently, impact tumour formation, growth and resistance. Bcl-2 is an important target in

haematological malignancies and could be studied in combination with anti-CD20 antibodies such as MabThera/Rituxan or obinutuzumab.

- **Obinutuzumab**, the first glyco-engineered humanised anti-CD20 monoclonal antibody, is currently being studied in a global phase III programme in chronic lymphocytic leukaemia and non-Hodgkin's lymphoma. Together with the BCl-2 inhibitor RG7601 and the anti-CD 22 antibody-drug conjugate RG7593, Roche has a strong set of assets in its development pipeline with the potential to further improve on MabThera/Rituxan, the current standard of care in fighting haematological tumours.

In addition to oncology, Roche is also focusing on neurodegenerative and psychiatric disorders such as Alzheimer's disease and schizophrenia, as well as on autoimmune and metabolic diseases.

Neuroscience: mechanism-based drug discovery in areas of high unmet need

Addressing untreated symptoms in schizophrenia: A global phase III programme of six studies exploring two indications is ongoing for **bitopertin**, an investigational first-in-class glycine reuptake inhibitor. The phase III programme is designed to optimise data quality by conducting three studies for negative symptoms and three studies for sub-optimally controlled symptoms in schizophrenia in parallel at the same clinical sites. A companion diagnostics assay is in development to validate the hypothesis for an exploratory biomarker predicting response to therapy with bitopertin. Data are expected in late 2013.

Multiple targets in Alzheimer's disease: Roche is pursuing a number of projects covering a broad range of approaches such as preventing the production of amyloid (BACE inhibitor RG7129), removing amyloid plaque (anti-Aβ monoclonal antibodies gantenerumab and crenezumab), and protecting tissue and blood vessels in the brain from oxidative stress (MAO-B inhibitor RG1577). **Gantenerumab**, which is furthest advanced in clinical development, is a human IgG1 monoclonal antibody with low potential for immunogenicity and a high binding affinity towards aggregated forms of amyloid beta (Aβ). Data from a phase I study showed that gantenerumab reduced Aβ amyloid plaque in the brains of patients with Alzheimer's disease (AD). Aβ amyloid plaque is found at high levels in the brains of people suffering from AD and is thought to be causally related to the pathogenesis of the disease. As Aβ plaque accumulates for decades prior to the clinical manifestation of AD, Roche's approach is to treat people early to prevent the onset of irreversible clinical symptoms and dementia. A phase II/III study called SCarlet RoAD in patients with prodromal AD was recently expanded to recruit 770 patients. To identify prodromal AD patients eligible for recruitment into SCarletRoAD, cerebrospinal fluid (CSF) Tau/Aβ levels are determined and

companion diagnostics assays based on (CSF) Tau/Aβ are in development. Data read-out for SCarlet RoAD is expected in 2015.
A second anti-Aβ monoclonal antibody, **crenezumab**, targeting oligomeric and fibrillar forms of amyloid, is in phase II testing to evaluate efficacy and safety in patients with mild to moderate AD. Crenezumab was selected for a landmark study aiming to prevent the onset of AD in a group of people whose genetic heritage causes them to develop the disease early in life.

Metabolic diseases: aleglitazar study AleNephro confirms renal safety profile

Aleglitazar is being investigated as a treatment for cardiovascular risk reduction in patients with type 2 diabetes who have experienced acute coronary syndrome (ACS) and are at very high risk for further cardiovascular (CV) events. The CV outcomes study AleCardio completed enrolment in May 2012 (with 7229 patients randomised). The study is event-driven and powered to show a 20% risk reduction in major adverse cardiac events in post-ACS patients with type 2 diabetes compared to standard of care. Data read-out is expected in 2015.
Newly obtained results from AleNephro, a phase II renal safety de-risking study for Aleglitazar in patients with type 2 diabetes and moderate renal impairment, showed that the study met its primary objective of no more than a mild decrease in renal function that was fully reversible.

Anti-PCSK9 (RG7652) is a monoclonal antibody directed against PCSK9 (proprotein convertase subtilisin/kexin type 9), a secreted protein that increases levels of low-density lipoprotein cholesterol (LDL-C) in the blood by promoting the degradation of LDL receptors in the liver. Inhibition of PCSK9 decreases circulating LDL-C, thereby potentially improving CV outcomes. As its mode of action differs from that of statins, anti-PCSK9 may provide benefit to people who do not achieve desirable LDL-C levels with statins or cannot tolerate them. A phase I study in healthy people with elevated LDL-C demonstrated significant decreases in LDL-C levels both with and without statin combination. A phase II study is ongoing to investigate different dosing schedules. Results are expected in 2013.

Immunology: improving response rates and treatment success through a personalised approach

Rontalizumab is a humanised anti-interferon-alpha (anti-IFN-α) antibody in development for moderately to severely active systemic lupus erythematosus (SLE). SLE is a chronic autoimmune disease, which involves multiple organ systems and severe forms of SLE can be life threatening. It represents a high unmet medical need, since current treatments either have severe side effects or are only mildly effective. A proof-of-concept phase II study with rontalizumab in SLE patients was designed with a biomarker

programme in place to identify the subpopulation of patients most likely to respond to anti-INF-α treatment. The study has been completed and the data will be presented at an upcoming medical conference later this year.

R&D investment: budget and resource allocation criteria

Roche's innovation-based strategy of combining Pharmaceuticals and Diagnostics under one roof has delivered a late-stage pipeline and growth opportunities that position the company well in continuing to create value for all stakeholders.

Roche will continue to allocate the biggest part of its R&D investment to oncology, given the sustained high level of unmet medical need and Roche's unsurpassed expertise in this area. However, the company remains committed to investing in other disease areas of high unmet medical need such as neuroscience, metabolism, inflammation and virology, whenever there are opportunities to significantly advance medical therapies.

At the same time Roche continues to improve R&D productivity by implementing rigorous portfolio prioritisation, innovative development designs, and cost saving measures. The recent initiative to streamline global pRED activities and to close the site in Nutley, New Jersey, frees up resources that will be reinvested in the growing pipeline allowing overall R&D expenditures to remain stable for the Group.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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