Forward-Looking Statements

This presentation may include forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. (the “Company”). These statements reflect the Company’s current analysis of existing information and trends. Actual results may differ from expectations based on risks and uncertainties that may affect the Company’s businesses.

Although this presentation includes information regarding pharmaceuticals (including products under development), the information is not intended as any advertisement and/or medical advice.
# Projects under Development (as of June 29, 2017)

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Filed</th>
</tr>
</thead>
</table>
| CKI27  
(Japan / overseas) 
- solid tumors |
RG7596 / polatuzumab vedotin  
- NHL |
RG7604 / taselisib  
- solid tumors |
RG7440 / ipatasertib  
- solid tumors |
GC33 (RG7686) / codrituzumab  
- HCC★ |
ERY974 (overseas)  
- solid tumors |
RG6078  
- solid tumors |
RG1273 / Perjeta  
- breast cancer (adjuvant)  
- gastric cancer |
RG3502 / Kadcyla  
- breast cancer (adjuvant) |
GA101 (RG7159) / obinutuzumab  
- indolent NHL |
RG435 / Avastin  
- RCC |
RG7446 / atezolizumab  
- NSCLC (adjuvant)  
- SCLC  
- urothelial carcinoma  
- MIUC (adjuvant)  
- RCC  
- RCC (adjuvant)  
- breast cancer  
- ovarian cancer  
- prostate cancer |
RG7446 / atezolizumab  
- NSCLC |
AF802 (RG7853) / Alecensa (overseas)  
- NSCLC [1L] |

In principle, completion of first dose is regarded as the start of clinical studies in each phase. 

Letters in orange: in-house projects
★: Multinational study managed by Chugai

**Oncology**

**NHL**: non-Hodgkin’s lymphoma  
**HCC**: hepatocellular carcinoma  
**NSCLC**: non-small cell lung cancer  
**SCLC**: small cell lung cancer  
**MIUC**: muscle invasive urothelial carcinoma  
**RCC**: renal cell carcinoma
ASCO2017
Key Presentations Featuring Chugai Projects

Alecensa® (alectinib)
- Alectinib versus crizotinib in treatment-naïve advanced ALK-positive non-small cell lung cancer: Primary results of the global phase III ALEX study [Abstract #LBA9008 (oral)]
- Updated efficacy and safety of the J-ALEX study comparing alectinib with crizotinib in ALK-inhibitor naïve ALK fusion positive non-small cell lung cancer study [Abstract #9064 (poster)]

Perjeta® (pertuzumab)
- APHINITY trial (BIG 4-11): A randomized comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with HER2-positive early breast cancer [Abstract #LBA500 (oral)]
ASCO2017
Key Presentations Featuring Chugai Projects

Atezolizumab

1. Non-Small Cell Lung Cancer (NSCLC)
   - Impact of atezolizumab treatment beyond disease progression (TBP) in advanced NSCLC: Results from the randomized phase III OAK study [Abstract #9001 (oral)]
   - Atezolizumab plus platinum-based chemotherapy (chemo) in non-small cell lung cancer: Update from a phase 1b study [Abstract #9092 (poster)]

2. Renal Cell Carcinoma
   - IMmotion 150: A phase II trial in untreated metastatic renal cell carcinoma patients of atezolizumab and bevacizumab vs and following atezo or sunitinib [Abstract #4505 (oral)]
ASCO2017
Key Presentations Featuring Chugai Projects

**Ipatasertib**

- LOTUS: A double-blind placebo-controlled randomized phase II trial of first-line ipatasertib + paclitaxel for metastatic triple-negative breast cancer (TNBC) [Abstract #1009 (poster discussion)]

**ERY974**

- A phase I dose escalation and cohort expansion study of ERY974, a T-cell redirecting bispecific antibody against Glypican 3 in patients with advanced solid tumors [Abstract #TPS3112 (poster)]

**CKI27**

- Results from the biomarker-driven basket trial of RO5126766 (CH5126766), a potent RAF/MEK inhibitor, in RAS- or RAF- mutated malignancies including multiple myeloma [Abstract #2506 (oral)]
Alecensa
ALEX Study: Study Design

- Stage IIIB/IV NSCLC
- ALK+ disease according to IHC test
- Treatment naïve
- ECOG PS 0–2
  (n=303)

Alectinib 600mg BID*
Crizotinib 250mg BID

1:1

Until PD, toxicity, withdrawal or death
Subsequent therapy and survival follow-up

Stratification factors
- ECOG PS (0/1 vs 2)
- Ethnicity (Asian vs non-Asian)
- CNS metastases at baseline (presence vs absence)

Primary endpoint
- PFS (investigator assessed)

Secondary endpoints
- PFS by IRC
- Time to CNS progression
- ORR
- DoR
- OS
- CNS ORR
- CNS DoR
- QoL
- Safety

Modified from Shaw A. et al, ASCO 2017; ECOG PS=Eastern Cooperative Oncology Group Performance Status; BID=twice daily dosing; CNS=central nervous system; PFS=progression free survival; IRC=independent review committee; ORR=overall response rate; DoR=duration of response

* Approved dosage of Alectinib in Japan is 300mg BID
Alecensa
ALEX Study: Efficacy

Primary endpoint: Investigator-assessed PFS

Modified from Shaw A. et al, ASCO 2017; HR=hazard ratio; NE=not estimable

* Approved dosage of Alectinib in Japan is 300mg BID
Alecensa
ALEX Study: Efficacy

Secondary endpoint: Time to CNS progression (by IRC, ITT)

Modified from Shaw A. et al, ASCO 2017; CNS=central nervous system; IRC=independent review committee; ITT=intent to treat;
*=12-month cumulative incidence rate

* Approved dosage of Alectinib in Japan is 300mg BID
Alecensa
ALEX Study: Safety
Adverse events, ≥10% between treatment arms

<table>
<thead>
<tr>
<th></th>
<th>Crizotinib (N=151)</th>
<th>Alectinib (N=152)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any grade</td>
<td>Grade 3–5</td>
</tr>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>72 (48)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>68 (45)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>58 (38)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>42 (28)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>29 (19)</td>
<td>0</td>
</tr>
<tr>
<td>ALT increased</td>
<td>45 (30)</td>
<td>22 (15)</td>
</tr>
<tr>
<td>AST increased</td>
<td>37 (25)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>18 (12)</td>
<td>0</td>
</tr>
<tr>
<td>Blood bilirubin increased</td>
<td>2 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>7 (5)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Weight increased</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Modified from Shaw A. et al, ASCO 2017; ALT=alanine aminotransferase; AST=aspartate transaminase

* Approved dosage of Alectinib in Japan is 300mg BID
Alecensa
J-ALEX: Study Design

- Patients with advanced ALK+ NSCLC were randomized 1:1 to receive oral ALC 300 mg BID or oral CRZ 250 mg BID until disease progression or unacceptable toxicity.
- Stratification factors were ECOG PS (0/1 vs. 2), treatment line (1st vs. 2nd), and clinical stage (IIIIB/IV vs. recurrent).

**STUDY DESIGN**

Key Entry Criteria
- ≥20 years of age
- Stage IIIb/IV or recurrent ALK+ NSCLC
- ALK centralized testing (IHC and FISH or RT-PCR)
- ECOG PS 0-2
- ≥1 measurable lesion assessed by investigator
- Treated/asymptomatic brain metastases allowed
- ≤1 prior chemotherapy

ALC 300 mg BID PO, 28-day cycle (n=103)

CRZ 250 mg BID PO, 28-day cycle (n=104)

Endpoints
- Primary
  - PFS assessed by IRF*
- Secondary
  - Overall survival (OS)
  - Objective response rate (ORR)
  - Duration of response
  - Time to response
  - CNS PFS
  - Health-related quality of life (HRQOL)
  - Safety
  - Pharmacokinetics (PK)

*IRF: Independent Review Facility

Modified from Takiguchi Y. et al, ASCO 2017; ALC=alectinib; CRZ=crizotinib; PO=by mouth
Alecensa
J-ALEX: Efficacy

Primary endpoint: PFS by IRF in the intent-to-treat (ITT) population

- The safety profiles were consistent with those seen in previous studies.

Modified from Takiguchi Y. et al, ASCO 2017
Pertuzumab
APHINITY: Study Design

Randomized phase III study in patients with HER2-positive early breast cancer

Primary endpoint: IDFS (Invasive Disease-Free Survival)
Secondary endpoints: IDFS including second primary non-breast cancer, disease-free interval, OS, safety, HRQoL

Stratification factors:
- Chemo regimen
- HR status
- Nodal status
- Geographic region
- Protocol version

* A limited number of standard anthracycline or non-anthracycline (TCH) regimens were allowed

Modified from Minckwitz G. et al, ASCO 2017
Pertuzumab
APHINITY: Primary Analysis (IDFS)

- The safety profiles were consistent with those seen in previous studies.

Modified from Minckwitz G. et al, ASCO 2017
Pertuzumab
APHINITY: Subgroup Analysis (Nodal Status)

Lymph node-negative subgroup (n = 1799)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Event-free proportion</th>
<th>IDFS</th>
<th>Pertuzumab (n = 897)</th>
<th>Placebo (n = 902)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>99.7%</td>
<td>99.5%</td>
<td>99.1%</td>
<td>99.0%</td>
</tr>
<tr>
<td>2 years</td>
<td>99.4%</td>
<td>98.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td>96.7%</td>
<td>96.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td>90.2%</td>
<td>90.2%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No. of patients at risk: 897 865 856 849 841 826 818 775 456

Lymph node-positive subgroup (n = 3005)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Event-free proportion</th>
<th>IDFS</th>
<th>Pertuzumab (n = 1503)</th>
<th>Placebo (n = 1502)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>98.1%</td>
<td>98.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 years</td>
<td>94.9%</td>
<td>93.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td>89.9%</td>
<td>86.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td>84.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No. of patients at risk: 1503 1444 1419 1387 1358 1327 1283 912 423

Events, n (%): Pertuzumab 32 (3.6) Placebo 29 (3.2)
Unstratified HR (95% CI): Pertuzumab 1.13 (0.68, 1.86)
p-value: 0.6436
Median Follow-up: 48.3 months

Modified from Minckwitz G. et al, ASCO 2017
Pertuzumab
APHINITY: Subgroup Analysis (HR Status)

HR-positive subgroup (n = 3082)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>IDFS</th>
<th>Pertuzumab (n = 1536)</th>
<th>Placebo (n = 1546)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>98.9%</td>
<td>99.3%</td>
<td>1.00 (0.66, 1.13)</td>
</tr>
<tr>
<td>2 years</td>
<td>96.5%</td>
<td>96.8%</td>
<td>1.00 (0.66, 1.13)</td>
</tr>
<tr>
<td>3 years</td>
<td>94.8%</td>
<td>94.4%</td>
<td>1.00 (0.66, 1.13)</td>
</tr>
<tr>
<td>4 years</td>
<td>93.0%</td>
<td>91.6%</td>
<td>1.00 (0.66, 1.13)</td>
</tr>
</tbody>
</table>

HR-negative subgroup (n = 1722)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>IDFS</th>
<th>Pertuzumab (n = 864)</th>
<th>Placebo (n = 858)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>98.1%</td>
<td>97.9%</td>
<td>1.00 (0.56, 1.04)</td>
</tr>
<tr>
<td>2 years</td>
<td>96.2%</td>
<td>93.7%</td>
<td>1.00 (0.56, 1.04)</td>
</tr>
<tr>
<td>3 years</td>
<td>92.8%</td>
<td>91.2%</td>
<td>1.00 (0.56, 1.04)</td>
</tr>
<tr>
<td>4 years</td>
<td>91.0%</td>
<td>88.7%</td>
<td>1.00 (0.56, 1.04)</td>
</tr>
</tbody>
</table>

Modified from Minckwitz G. et al, ASCO 2017; HR=hormone receptor
Ipatasertib
LOTUS: Study Design

Double-blind placebo controlled randomized phase II study

- Inoperable locally advanced/metastatic TNBC
- No prior systemic therapy for advanced/metastatic disease (n = ~120)

Stratification Factors
- (Neoadjuvant chemotherapy* (yes vs no)
- Chemotherapy-free interval (≤12 vs >12 months vs no prior chemo)
- Tumor PTEN status (H-score 0 vs 1-150 vs >150, by TARGOS)

Primary Endpoints
- PFS in ITT population
- PFS in PTEN-low subgroup (by Ventana IHC)

Secondary Endpoints
- ORR, DoR and OS in all patients and PTEN-low subgroup
- PFS, ORR, DoR and OS in FMI NGS Dx+ subgroup (PI3K/Akt pathway-activated tumors)
- Safety and tolerability

Modified from Dent R. et al, ASCO 2017; TNBC=triple-negative breast cancer; PTEN=phosphatase and tensin homolog; FMI=Foundation Medicine, Inc.; NGS=next-generation sequencing
Ipatasertib
LOTUS: Efficacy (PFS)

ITT population

PIK3CA/AKT1/PTEN-altered
tumor population

Modified from Dent R. et al, ASCO 2017
ERY974 (TRAB)

- Humanized IgG4 monoclonal antibody
- Fc region mutated to reduce non-specific cytokine release
- Plasma T1/2 is expected to be 2-5 days

Multicenter, international Phase I dose escalation and cohort expansion study

**Study objectives**
- Determination of dose limiting toxicities (DLTs) and establishing recommend dose (RD)
- Evaluate anti-tumor efficacy in 3 tumor type specific cohorts treated at the RD

**Ongoing dose escalation cohort**
- No DLT is observed
- Cytokine release syndrome with IL-6 elevation is observed
- Dose escalation is ongoing

Modified from Hashimoto K. *et al*, ASCO 2017; TRAB=T-cell redirecting antibody
Efficacy of ERY974 in Preclinical Models

(Sano Y. et al., AACR2017)

ERY974 monotherapy (KYSE70)

ERY974 + PD-L1 Ab (Hepa1-6/hGPC3)

ERY974 + paclitaxel (NCI-H446)
CKI27
Potent RAF/MEK Inhibitor in $\text{KRAS}^{\text{mut}}$ NSCLC and $\text{KRAS}^{\text{mut}}/\text{BRAF}^{\text{mut}}$ Gynaecological Cancers

Modified from Chenard-Poirier M. et al, ASCO 2017; CH5126766=CKI27
Targeting Treatment Options to Different Patients and Cancer Types

**IMMUNE INFLAMED**
- CD8+ T cells infiltrated, but non-functional
- Accelerate or remove brakes on T-cell response
  - e.g. Tecentriq, Cotellic, navoximod (IDOi), aOX40, aTIGIT, aCEA/FAP
  - IL-2v, aCSF-1R, TCBs (CEA TCB, CD20 TCB), TRAB (ERY974)

**IMMUNE EXCLUDED**
- CD8+ T cells accumulated but have not efficiently infiltrated
- Bring T-cells in contact with cancer cells
  - e.g. aVEGF, TCBs (CEA TCB, CD20 TCB), TRAB (ERY974)

**IMMUNE DESERT**
- CD8+ T cells absent from tumor and periphery
- Increase number of antigen-specific T-cells or increase antigen presentation
  - e.g. aCD40, chemotherapy, radiotherapy, targeted therapies, TCBs (CEA TCB, CD20 TCB), TRAB (ERY974), PCV

TCB=T cell bispecific; TRAB=T-cell redirecting antibody; PCV=personalized cancer vaccine
Contacts: Corporate Communications Dept.

Investor Relations Group
Tel: +81 (0)3-3273-0554  Fax: +81 (0)3-3281-6607
e-mail: ir@chugai-pharm.co.jp
Toshiya Sasai, Takayuki Sakurai, Tomoko Shimizu,
Tomoyuki Shimamura