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Chugai Obtains Approval for Expanded Use of FoundationOne CDx Cancer Genomic Profile as a Companion Diagnostic for Olaparib in *BRCA*-Mutated Prostate Cancer

- FoundationOne CDx approved as a companion diagnostic to identify prostate cancer who may be appropriate for treatment with olaparib
- Olaparib was approved on December 25 for the treatment of *BRCA*-mutated castrate-resistant prostate cancer with distant metastasis

TOKYO, December 28, 2020 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it obtained approval from the Ministry of Health, Labour and Welfare (MHLW) on November 4, 2020, for the expanded use of FoundationOne® CDx Cancer Genomic Profile as a companion diagnostic for the PARP inhibitor, Lynparza® (generic name: olaparib) for the treatment of *BRCA*-mutated castrate-resistant prostate cancer with distant metastasis (mCRPC).

“We are pleased that FoundationOne CDx Cancer Genomic Profile was approved as a companion diagnostic of olaparib for prostate cancer,” said Dr. Osamu Okuda, Chugai’s President and COO. “In addition to ovarian cancer, the significance of detecting *BRCA1/2* alterations and selecting the appropriate treatment for prostate cancer has become apparent. Through FoundationOne CDx Cancer Genomic Profile, we are committed to promoting the appropriate use of comprehensive genomic profiling to ensure that proper treatment will be provided to patients who may benefit from olaparib.”

The approval aims to expand FoundationOne CDx Cancer Genomic Profile for use as a companion diagnostic to identify prostate cancer patients with *BRCA1/2* alterations who could benefit from the treatment with olaparib whose disease progressed after treatment with enzalutamide or abiraterone by detecting *BRCA1/2* gene alterations. The efficacy and safety of olaparib in mCRPC patients with *BRCA1/2* alterations were investigated in the Phase III PROfound study and AstraZeneca K.K. received approval from the MHLW on December 25. Olaparib is jointly developed and commercialized by AstraZeneca (LSE/STO/Nasdaq: AZN) and MSD (Merck Sharp & Dohme Corp, a subsidiary of Merck & Co., in the US and Canada).

As a leading company in the field of oncology, Chugai is committed to realize advanced personalized oncology care and contribute to patients and healthcare professionals through improving access to comprehensive genomic profiling.

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Approval information The underlined part has been newly added.

Intended uses or indications

- The Product is used for comprehensive genomic profiling of tumor tissues in patients with solid cancers.
- The Product is used for detecting gene mutations and other alterations to support the assessment of drug indications listed in the table below.

Alterations	Cancer type	Relevant drugs
Activated *EGFR* alterations	Non-small cell lung cancer (NSCLC)	afatinib dimaleate, erlotinib hydrochloride, gefitinib, osimertinib mesylate
EGFR exon 20 T790M alterations		osimertinib mesylate
ALK fusion genes		alectinib hydrochloride, crizotinib, ceritinib
ROS1 fusion genes		entrectinib
MET exon 14 skipping alterations		capmatinib hydrochloride hydrate
BRAF V600E and V600K alterations	Malignant melanoma	dabrafenib mesylate, trametinib dimethyl sulfoxide, vemurafenib
ERBB2 copy number alterations (HER2 gene amplification positive)	Breast cancer	trastuzumab (genetical recombination)
KRAS/*NRAS* wild-type	Colorectal cancer	cetuximab (genetical recombination), panitumumab (genetical recombination)
NTRK1/2/3 fusion gene	Solid tumors	entrectinib
BRCA1/2 alterations	Ovarian cancer	olaparib
BRCA1/2 alterations	Prostate cancer	olaparib

About FoundationOne CDx Cancer Genomic Profile

Developed by Foundation Medicine Inc., FoundationOne CDx Cancer Genomic Profile is a next-generation sequencing based *in vitro* diagnostic device for the detection of substitutions, insertion and deletion alterations, and copy number alterations in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue specimens. The program is available as a companion diagnostic for multiple molecular-targeted drugs approved in Japan.

About *BRCA* alterations

BRCA1 and *BRCA2* are human genes that produce proteins responsible for repairing damaged DNA and play an important role in maintaining the genetic stability of cells. When either of these genes is mutated or altered, such that its protein product either is not made or does not function correctly, DNA damage may not be

repaired properly, and cells become unstable. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer and confer sensitivity to PARP inhibitors including Lynparza.[1-4]

[Reference]

1: Kirby, M. (2011). Characterising the castration-resistant prostate cancer population: a systematic review. International Journal of Clinical Practice, 65(11), pp.1180-1192.
2: Wu J, et al. (2010) The role of BRCA1 in DNA damage response. Protein Cell. 2010;1(2):117-123.
3: Roy R, et al. (2012). BRCA1 and BRCA2: different roles in a common pathway of genome protection. Nat Rev Cancer. 2011;12(1):68-78. Published 2011 Dec 23. doi:10.1038/nrc3181.
4: Gorodetska I, et al. (2019). BRCA Genes: The Role in Genome Stability, Cancer Stemness and Therapy Resistance. J Cancer. 2019;10(9):2109-2127.

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