Study shows that selection of breast cancer patients for adjuvant bisphosphonate therapy based on Inbiomotion's MAFTEST® reduces the risk of death in comparison with current clinical guidance

- MAFTEST® analyses of the NSABP-B34 and AZURE landmark clinical trials confirmed clinical utility of the MAFTEST® for selection of early-stage breast cancer patients that benefit from adjuvant clodronate treatment.
- Reduces the risk of death at 5 and 10 years by 26% and 23% respectively.
- Identifies almost twice as many patients able to benefit from the intervention than are selected using current clinical guidelines.
- Data published in *Annals of Oncology,* (*33), SUPPLEMENT 3, S152, 2022*.

Barcelona, July 14 2022; Inbiomotion SL, a company developing a unique single-gene-based biomarker for the personalized adjuvant treatment of early-stage (stage I-III) breast cancer patients, announces the results of comparing the clinical efficacy of implementing the proprietary MAFTEST® for selection of patients for adjuvant bisphosphonates therapy with current clinical guidance. The results were presented at the ESMO 2022 Breast Cancer Symposium.

The data show that stratification of early breast cancer patients according to **MAF status reduced the risk of death and relapse in MAF negative patients by 26% and 23% respectively**, compared to a 12% and 15% reduction in the risk of death or relapse seen with stratification by menopausal status recommended by current ESMO and ASCO Clinical Guidelines. The data also indicate that adjuvant treatment with bisphosphonates should be avoided in MAF positive patients as the risk of death and relapse is increased 16% and 15% respectively in these patients.

In addition, the study shows that the use of MAF status for selection of early breast cancer patients for treatment with bisphosphonates allows the treatment of young premenopausal patients currently excluded by existing clinical guidance.

"The MAF biomarker allows a new paradigm for selection of patients for adjuvant bisphosphonate treatment of early breast cancer that not only identifies those patients that will benefit from treatment (MAF negatives) but also excludes patients that could be harmed (MAF positives). This new selection criteria not only reduces the risk of death and relapse for selected patients but also provides a new treatment option for young patients currently excluded from this treatment in current clinical practice.", **said Robert Coleman, Professor Emeritus, Department of Oncology and Metabolism, University of Sheffield, UK.**

Currently, clodronate and other bisphosphonates are not approved by the regulatory agencies for use in adjuvant treatment of the broad population of early-stage breast cancer patients. However, they are recommended in the ASCO/CCO and ESMO clinical guidelines for adjuvant treatment of breast cancer in postmenopausal patients. The study shows that identifying MAF-negative patients for selection for adjuvant treatment with bisphosphonates outperforms current selection by menopausal status and could give more patients, particularly younger patients, the opportunity to benefit from adjuvant bisphosphonates, while avoiding potential harm (or no benefit), than solely using menopausal status as a selection criterion.

"Our results indicate that adjuvant clodronate treatment has a large clinical benefit if restricted to MAF-negative patients.", **said Prof. Alexander Paterson, principal investigator of the NSABP-B34 clinical trial and Emeritus Clinical Professor at the Department of Oncology, University of Calgary**. "Our data provide an objective criterion for patient selection for bisphosphonate adjuvant treatment that outperforms current selection based on menopausal status".

"This study confirms our previous findings and the clinical utility of MAFTEST® as a unique tool for precision medicine in early breast cancer. Every year approximately 355,000 women are diagnosed with early breast cancer in Europe with a 10% risk of death at 5 years. Using MAF Test these deaths could be reduced by 26%, which would translate to 9,230 lives saved.", **said Joël Jean-Mairet, Executive Chairman of the Board of Inbiomotion**.

"We have discovered and developed a new biomarker, MAF gene amplification, that if used as selection criteria for adjuvant treatment with bisphosphonates improves the clinical outcome of

breast cancer patients compared with current clinical practice**", said Prof. Roger Gomis, ICREA Research Professor at IRB Barcelona**. "MAF Test is a biomarker that is easy to implement in any clinical pathology lab and should be considered for routine characterization of breast cancer tumors".

Recently the MAFTEST® obtained the CE-mark as an in vitro diagnostic medical device for **prognostic** purposes. Since clodronate and other bisphosphonates are not approved by the regulatory agencies for use in adjuvant treatment of early-stage breast cancer patients, Inbiomotion's MAFTEST® is not authorized to be used as a companion diagnostic as described in the above-mentioned study.

Reference articles:

Impact of MAF selection of patients for adjuvant bisphosphonate therapy and comparison with current clinical guidance Robert Coleman, Roger R Gomis, Alexander H G Paterson.

Full text article: https://www.annalsofoncology.org/article/S0923-7534(22)00461-6/fulltext

MAF amplification and adjuvant clodronate outcomes in early-stage breast cancer in NSABP B-34 and potential impact on clinical practice Alexander H G Paterson et al.

Full text article: https://pubmed.ncbi.nlm.nih.gov/34377934/

Effect of MAF amplification on treatment outcomes with adjuvant zoledronic acid in early breast cancer: a secondary analysis of international, open-label, randomized, controlled, phase 3 AZURE (BIG 01/04) trial Robert Coleman et al.

Full text article: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(17)30603-4/fulltext

Benefits and risks of adjuvant treatment with zoledronic acid in stage II/III breast cancer. 10 years follow-up of the AZURE randomized clinical trial (BIG 01/04) Robert Coleman et al.

Full text article: https://pubmed.ncbi.nlm.nih.gov/30591866/

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Notes to Editors:

About Inbiomotion:
Inbiomotion SL, a company founded by Prof. Roger Gomis, is developing a unique single gene-based biomarker for the personalized adjuvant treatment of early-stage breast cancer patients. The biomarker has been technically and analytically validated. The results of the first trial using well annotated archived specimens of the AZURE registrational clinical trial, now confirmed in the NSABP-B34 trial, indicate its potential use as a companion diagnostic. The company holds over 200 patents and patent applications covering its proprietary FISH MAFTEST® and the use of bisphosphonates in the adjuvant treatment of early-stage breast cancer patients.

About MAF:
MAF (mesenchymal aponeurotic fibrosarcoma gene, an AP-1 family transcription factor) is expressed in primary cancer tumors. This is associated with increased metastasis, especially bone metastasis. MAF transcriptionally controls genes such PTHrP, which regulate metastasis-related cellular processes, including survival, initiation, metabolic rewiring, and particularly, adhesion to bone marrow–derived cells and osteoclast differentiation. These observations point to MAF having a key hierarchical role in metastasis.