Hospital Administrators, Insurance Payers, and Medical Providers,

We are writing to respectfully encourage patient care providers and payers to ensure that all primary and metastatic brain tumor tissue is promptly sent out for comprehensive biomarker testing and urgent processing in order to receive an accurate diagnosis.

- Molecular testing is mandatory for complete diagnosis and treatment guidance
- Testing should be done as soon possible and as thorough as possible
- Testing should receive strong insurance coverage and done at lowest possible cost

Patients with primary and metastatic brain and spinal tumors deserve care that reflects the most current scientific evidence and clinical best practices in neuro-oncology. The central nervous system (CNS) experiences a wide variety of tumors that are complex and are characterized by significant heterogeneity and limited successful treatment options. Biomarker testing provides critical information about a tumor's molecular characteristics, helping guide accurate diagnosis, prognosis, treatment selection, and determine eligibility for clinical trials. Patients may miss timely access to life-extending or life-saving therapies without this testing.

Thorough molecular testing is crucial for understanding the biological complexities of the tumor<sup>2</sup>, determining what clinical trials a patient may be eligible for and benefit from, and for developing personalized treatment strategies. For example, gliomas with only lower grade histologic features can be upgraded to CNS WHO grade 4 glioblastoma by molecular testing; thus, routine screening of all gliomas for these markers is now considered mandatory. Conversely, a tumor resembling glioblastoma may have genetic alterations and DNA methylation profiles that change the diagnosis to less aggressive entities. An accurate diagnosis as determined by **proper tumor testing can drastically shape clinical trial options and treatment decisions** and is necessary to avoid over- or under-treating the disease.

We aim to emphasize the following to all centers involved in the care of these patients:

After a biopsy or surgical removal, tumor tissue should be sent out for biomarker testing immediately. According to a recent article titled *Molecular Testing for the World Health Organization Classification of Central Nervous System Tumors*, published in JAMA Oncology and co-authored by expert neuropathologists, "The newest edition of the World Health Organization (WHO) classification

<sup>&</sup>lt;sup>1</sup> Weller M, van den Bent M, Preusser M, Le Rhun E, Tonn JC, Minniti G, Bendszus M, Balana C, Chinot O, Dirven L, French P, Hegi ME, Jakola AS, Platten M, Roth P, Rudà R, Short S, Smits M, Taphoorn MJB, von Deimling A, Westphal M, Soffietti R, Reifenberger G, Wick W. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. Nat Rev Clin Oncol. 2021 Mar;18(3):170-186. doi: 10.1038/s41571-020-00447-z. Epub 2020 Dec 8. Erratum in: Nat Rev Clin Oncol. 2022 May;19(5):357-358. doi: 10.1038/s41571-022-00623-3. PMID: 33293629; PMCID: PMC7904519.

<sup>&</sup>lt;sup>2</sup> Brat DJ, Aldape K, Bridge JA, Canoll P, Colman H, Hameed MR, Harris BT, Hattab EM, Huse JT, Jenkins RB, Lopez-Terrada DH, McDonald WC, Rodriguez FJ, Souter LH, Colasacco C, Thomas NE, Yount MH, van den Bent MJ, Perry A. Molecular Biomarker Testing for the Diagnosis of Diffuse Gliomas. Arch Pathol Lab Med. 2022 May 1;146(5):547-574. doi: 10.5858/arpa.2021-0295-CP. PMID: 35175291; PMCID: PMC9311267.

of CNS tumors includes tumors that now require detection of specific molecular alterations. When integrated with histology, the entire spectrum of CNS tumors can now be diagnosed using one or more molecular tests, including next-generation sequencing (NGS), genomic copy number array, fusion screening, and genomic DNA methylation profiling."<sup>3</sup> This comprehensive diagnostic approach typically requires a combination of testing methods as determined by a neuropathologist.

The timing and cost of tumor testing are key aspects to consider as both can greatly impact access and outcome. Standard of care for treatment for malignant brain tumors should begin 4-6 weeks after surgery. Today, the critical testing itself can take 2-3 weeks to obtain results. Additional time delays occur in most practices (especially community hospitals where there is no access to in-house sequencing available in many academic centers), because of the 2018 Medicare 14-day rule that bills on the day of testing rather than the day of tumor collection. Patients have an urgent need to receive accurate results as soon as possible to make informed decisions for their care and to emotionally process their diagnosis. Biomarker testing costs less than 2% of total CNS tumor care and has an outsized impact on whether and how the other 98% is spent. These clinically essential tools should be offered at the lowest cost possible and receive strong coverage by insurance policies. Any systematic process or financial barriers that could delay receiving tumor testing results should be addressed and corrected as needed to avoid unnecessary negative impact on patients.

In order to provide patients with the best possible outcomes based on strong evidence-based justification, we encourage your support of any action in making sure that all primary and metastatic tumor tissue is promptly sent out for comprehensive biomarker testing and urgent processing. This testing is not optional. **Testing is the standard of care**, and it ensures that every patient has access to the most informed and effective treatment options available.

On behalf of the SNO Community Neuro-Oncology Committee,

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<sup>&</sup>lt;sup>3</sup> Horbinski C, Solomon DA, Lukas RV, Packer RJ, Brastianos P, Wen PY, Snuderl M, Berger MS, Chang S, Fouladi M, Phillips JJ, Nabors B, Brat DJ, Huse JT, Aldape K, Sarkaria JN, Holdhoff M, Burns TC, Peters KB, Mellinghoff IK, Arons D, Galanis E. Molecular Testing for the World Health Organization of Central Nervous System Tumors: A Review. JAMA Oncol. 2025 Mar 1;11(3):317-328. doi: 10.1001/jamaoncol.2024.5506. PMID: 39724142