ASSESSMENT

concerning the application materials for the competition to fill the academic position of "Professor," professional field 4.2 Chemical Sciences, scientific specialty "Bioorganic Chemistry, Chemistry of Natural and Biologically Active Substances," for the needs of Section "Molecular Design and Biochemical Pharmacology," as published in the State Gazette, Official Issue No. 114, 24 December 2025.

Candidate: Assoc. Prof. Nikolay Tsvetkov Tsvetkov, PhD

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I. Brief Biographical Information on the Candidate

Assoc. Prof. Nikolay Tsvetkov Tsvetkov was born on 18 October 1972 in Sofia. He graduated from the University of Chemical Technology and Metallurgy (UCTM), Sofia, with a degree in Chemical Technologies, specialization in Organic Synthesis Technology, earning the qualification of Master of Engineering (1999). His diploma thesis was carried out at the Hamburg University of Technology (TUHH) in Hamburg-Harburg, Germany.

Between 1999 and 2005, he completed his doctoral studies in the Department of Organic Chemistry I at the Faculty of Chemistry, Bielefeld University, Germany, where he successfully defended his dissertation entitled "Photoreactions of Tricyclic Cyclopropyl Ketones: Construction of Polyquinane and Analogous Ring Systems," receiving the degree of Doctor of Natural Sciences (Dr. rer. nat.) with a specialization in organic synthetic chemistry and photochemistry. Recognition of his doctoral degree in Bulgaria was certified by Certificate No. 000063, dated 16 March 2018.

From 2008 to 2013, he held the position of Research Scientist–Lecturer at the BioPharma NeuroAlliance Consortium, Bonn (in partnership with UCB Pharma S.A., Belgium), where he led a synthesis laboratory for biologically active compounds and supervised pharmacy students. Concurrently, from 2011, he served as External Project Manager at UCB Pharma S.A. in the area of parallel synthesis of libraries of biologically active compounds. In the period 2014–2015, he was a part-time research and development project manager at Beraterm AG, Pratteln (Basel), Switzerland. From 2014 to 2017, he held the position of Senior Research Scientist–Lecturer at the Institute of Pharmacy, University of Bonn (Rheinische Friedrich-Wilhelms-Universität Bonn), where he led a laboratory for the physicochemical characterization of biologically active substances.

Since October 2017, he has been employed at the Institute of Molecular Biology "Acad. Roumen Tsanev" of the Bulgarian Academy of Sciences (IMB–BAS). Since July 2018, he has held the academic position of Associate Professor in Section "Molecular Design and Biochemical Pharmacology," and since January 2019 he has also served as Head of that section.

His experience as an external project manager for a global pharmaceutical leader such as UCB Pharma (Belgium) is evidence of his ability to translate fundamental scientific discoveries into practical applications in drug development — a skill of key importance for Section "Molecular Design and Biochemical Pharmacology," for the Institute, and for Bulgarian science as a whole.

II. Publication Activity and Compliance with the Requirements of the PZRASRB

The total number of scientific publications by Assoc. Prof. Tsvetkov is 101, of which 77 were published after his appointment to the academic position of Associate Professor at IMB–BAS (2018–2025). For the competition for the academic position of Professor, the candidate submits 5 scientific publications equivalent to a habilitation thesis (Group B, Indicator 4), in which he is the leading author and/or corresponding author, and 15 scientific publications (Group D, Indicator 7). Among all habilitation publications submitted for the competition, 15 are in Q1 journals and 5 are in Q2 journals according to SJR/JCR metrics, including the *European Journal of Medicinal Chemistry* and *Frontiers in Molecular Neuroscience* — prestigious international journals in the fields of medicinal chemistry and neuroscience.

According to the detailed compliance report submitted against the minimum national requirements and the requirements of IMB–BAS, Assoc. Prof. Tsvetkov has achieved a total of 1,338 points against a required minimum of 640 points. The distribution by indicator is as follows: Indicator A — 50 pts. (required minimum: 50 pts.); Indicator B4 — 120 pts. (required minimum: 100 pts.); Indicator D7 — 350 pts. (required minimum: 220 pts.); Indicator E11 — 624 pts. (required minimum: 120 pts.); Indicators F15–18 — 194 pts. (required minimum: 150 pts.).

Particularly noteworthy is the citation indicator group (E), reflecting 624 points against a required minimum of 120. The candidate's exceptionally high citation count (over 6,380 citations in Scopus) is particularly striking, yielding an impressive h-index of 25. These figures far exceed the minimum requirements for the position of Professor and place Assoc. Prof. Tsvetkov among the leading scientists in his field at the international level.

The candidate demonstrates an outstanding ability to attract funding and foster international collaboration. He serves as Principal Investigator on two projects funded by the Bulgarian National Science Fund (BNSF) and is an active participant in large-scale international networks such as PAPRIKANET.IT (EU Regional Development Programme, co-funded by the Italian Government and the Regional Government of Basilicata) and COST Actions (e.g., CA18202 and CA22105, not included in the competition application), which underscores his leadership role in the scientific community.

On the basis of the foregoing, Assoc. Prof. Tsvetkov fully meets and substantially exceeds the minimum requirements across all indicators for the academic position of Professor.

III. Scientific Contributions

The research of Assoc. Prof. Tsvetkov lies in the field of bioorganic and medicinal chemistry, with a focus on the rational design, synthesis, and biological evaluation of novel biologically active molecules for the treatment of neurodegenerative diseases (NDD), primarily Alzheimer's disease (AD) and Parkinson's disease (PD). His contributions can be systematized into the following thematic areas:

III.1. Design and Synthesis of Novel Reversible and Selective MAO-B Inhibitors with Multitarget Activity

A central theme in the scientific work of Assoc. Prof. Tsvetkov is the development of new-generation reversible and selective inhibitors of MAO-B — a key neuroenzyme whose elevated activity is associated with reduced dopamine levels in the brain, the generation of toxic reactive oxygen species, and ultimately, neuronal cell death. Currently approved in clinical practice are irreversible MAO-B inhibitors and second-generation reversible MAO-B inhibitors, both of which display unsatisfactory efficacy as standalone therapeutic agents and carry risks upon long-term use. The development of new-generation reversible MAO-B inhibitors is one of the priority scientific challenges in the field.

A series of reversible MAO-B inhibitors with exceptionally high potency and selectivity has been developed. The lead compound from this series — NTZ-2020 (compound 14) — is characterized by hMAO-B IC_{50} = 1.11 nM, K_i = 0.56 nM, and >9,000-fold selectivity over the MAO-A enzyme — parameters that surpass those of the clinically used safinamide. In addition to its excellent inhibitory profile, NTZ-2020 exhibits a neuroprotective effect on the viability of cortical neurons and stimulates neuronal network growth. Its ability to penetrate the blood–brain barrier has been confirmed in a cellular neurovascular unit model.

These studies included the first comparative investigation of two structurally related compound classes — indazole-5-carboxamides and (indazol-5-yl)methanimines — as reversible MAO-B inhibitors with multitarget activity. K_i values in the picomolar range (down to 170 pM) were established, with exceptional selectivity (SI > 25,000 over MAO-A). The structure–activity relationship was elucidated through single-crystal X-ray diffraction analysis (SCXRD), quantum-chemical calculations, and molecular modeling. These compounds represent promising lead structures for the development of drug candidates against AD, PD, and related NDDs.

III.2. Scientometric Analysis of MAO Enzymes as Biological Targets in Neuroscience

An in-depth bibliometric analysis was conducted of the scientific literature devoted to MAO as a privileged class of neuroenzymes with a key role in neurodegeneration. Through systematic analysis of the Web of Science Core Collection database, global trends in the development of this research field were identified — including leading authors, institutions, thematic priorities, and historical roots. The analysis was published in *Frontiers in Molecular Neuroscience* (Q1) and provides a valuable systematization of knowledge, outlining the prospects for developing multi-target therapeutics against NDDs.

III.3. Natural Products and Biologically Active Compounds — Physicochemical Characterization and Applications

Within the scientific activities of Section “Molecular Design and Biochemical Pharmacology,” Assoc. Prof. Tsvetkov also develops a line of research on natural products and biologically active substances with therapeutic potential. Work in this thematic group includes the physicochemical characterization and biological evaluation of diverse classes of natural and semi-synthetic compounds against enzymatic and receptor targets associated with neurodegenerative and oncological diseases.

IV. Conclusion

Assoc. Prof. Nikolay Tsvetkov Tsvetkov is a scientist with extensive international experience, acquired at leading European universities and pharmaceutical industry institutions. His scientific contributions in the fields of medicinal and bioorganic chemistry are original and consistently directed toward addressing pressing, socially significant challenges in the treatment of neurodegenerative diseases. The new-generation MAO-B inhibitors developed by the candidate — with picomolar activity, high selectivity, and favorable blood–brain barrier permeability — represent a significant scientific contribution that has received international recognition, as evidenced by the candidate's high citation metrics. His profound methodological expertise, combined with broad practical experience in research and development in the pharmaceutical industry, constitutes a strong asset for the research activities of Section "Molecular Design and Biochemical Pharmacology." Given the candidate's demonstrated project management capacity and international visibility, I am convinced that the appointment of Assoc. Prof. Tsvetkov as Professor will provide impetus for new collaborations with the pharmaceutical sector and will enhance the prestige of IMB–BAS as a center of innovation in bioorganic chemistry.

Based on the foregoing, I confidently recommend that the distinguished scientific jury vote in favor of the appointment of Assoc. Prof. Nikolay Tsvetkov Tsvetkov to the academic position of Professor in professional field 4.2 Chemical Sciences, scientific specialty "Bioorganic Chemistry, Chemistry of Natural and Biologically Active Substances."

SIGNATURE: