TO THE CHAIRMAN OF THE SCIENTIFIC JURY
Appointed by Order No. 15-05-169/11.08.2025
of the Executive Director and Procurator of
"Acibadem City Clinic Tokuda Hospital" JSC
Based on a decision of the Scientific Council
Protocol No. 59/10.07.2025

OPINION
From Assoc. Prof. Lachezar Boyanov Lozanov, Ph.D.

Head of the Department of Internal Medicine (Endocrinology and Nephrology),
"Acibadem City Clinic Tokuda Hospital" JSC

REGARDING: The dissertation entitled *"The Role of Fibroblast Growth Factor 23 in the Development of Renal Bone Disease and Cardiovascular Complications in Patients with Chronic Kidney Disease"* for obtaining the educational and scientific degree "Doctor,"
Higher Education Area 7: Healthcare and Sports,
Professional Field 7.1: Medicine,
Doctoral Program "Internal Medicine" by Dr. Dilyana Mihaylova Nikolova—independent doctoral student at the Department of Internal Medicine, "Acibadem City Clinic Tokuda Hospital" JSC,
Supervisor: Assoc. Prof. Alexander Ivanov Osichenko, M.D., Ph.D.

Dear Members of the Scientific Jury,
Chronic kidney diseases represent a serious medical and social problem. Among them, renal bone disease and cardiovascular diseases are leading factors in deteriorating quality of life and increased mortality in these patients.

In recent years, fibroblast growth factor 23 (FGF23)—a hormone that plays a key role in regulating phosphate and vitamin D metabolism—has drawn the attention of the scientific community. In chronic kidney disease, its persistently elevated levels are associated not only with the development of renal bone disease but also with numerous adverse cardiovascular effects. These findings make FGF23 "the missing piece of the puzzle" in the pathogenesis of bone–mineral disorders, a potential biomarker and therapeutic target, whose better understanding would be important for developing new strategies for prevention and treatment.

In this context, Dr. Dilyana Mihaylova Nikolova's dissertation on *"The Role of Fibroblast Growth Factor 23 in the Development of Renal Bone Disease and Cardiovascular Complications in Patients with Chronic Kidney Disease"* is of exceptional relevance. It aligns with the contemporary paradigm of an integrated approach to CKD patients, which examines not only classical biochemical markers but also new hormonal regulators to enable early risk identification and personalized therapeutic decisions.

The dissertation is substantial—106 printed pages—following the standard sections for a dissertation, well illustrated with 34 figures and 9 tables, citing 129 references (8 by Bulgarian authors and 121 by foreign authors). It is correctly formulated and structured.

The aim is clearly and precisely defined. A large cohort of 103 patients treated in the Nephrology Department of the Internal Medicine Clinic at Acibadem City Clinic Tokuda Hospital over a two-year period was studied. All six assigned tasks were completed, and the analysis of the results allowed the research goal to be achieved. Thirteen conclusions and seven contributions with original and significant scientific potential were formulated. The abstract meets academic requirements and reflects the dissertation's content.

The dissertation demonstrates that the rise of FGF23 begins in the early stages of CKD, which is associated with a faster increase in albuminuria and a more rapid progression of CKD. Therefore, therapy for bone–mineral disorders should begin in the early phases of the disease—an insight of significant practical value. The work has an important multidisciplinary orientation, providing recommendations for endocrinologists to refrain from calcium supplementation for PTH correction in treating patients with diabetes and CKD, as well as discussing the benefits and risks of treatment with calcitriol.

The doctoral candidate has systematically participated with original publications on the topic, presented findings at scientific conferences, and fulfilled all necessary requirements.

CONCLUSION:
The submitted documents and the dissertation *"The Role of Fibroblast Growth Factor 23 in the Development of Renal Bone Disease and Cardiovascular Complications in Patients with Chronic Kidney Disease"* meet all requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria (ЗРАСРБ), its Implementing Regulations, and the specific requirements adopted under the Rules of "Acibadem City Clinic Tokuda Hospital" JSC. No plagiarism was detected.

The dissertation of Dr. Dilyana Mihaylova Nikolova is relevant and up-to-date and properly structured. The design of the individual studies and the overall research approach correspond to the stated goals and tasks. The materials and methods are well chosen and precisely executed. The conclusions are justified and follow logically from the obtained results.

In view of the above, I confidently give my POSITIVE evaluation of the dissertation and propose to the Honorable Scientific Jury to award the educational and scientific degree "Doctor" in Higher Education Area 7: Healthcare and Sports, Professional Field 7.1: Medicine, Doctoral Program "Internal Medicine," to Dr. Dilyana Mihaylova Nikolova, for which I firmly vote "YES."

Sofia, 19.08.2025

Prepared by:
Assoc. Prof. Lachezar B. Lozanov, Ph.D.
Head of the Department of Internal Medicine