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

OPINION / STATEMENT

From Assoc. Prof. Dr. Daniela Yordanova Petrova, PhD
Associate Professor, Clinic of Nephrology
Military Medical Academy, Sofia

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"* submitted for the educational and scientific degree of Doctor, in the field of Higher Education 7. Health and Sports, professional area 7.1. Medicine, doctoral program *Internal Medicine* by Dr. Dilyana **Mihaylova** Nikolova, doctoral student in independent study at the Clinic of Internal Medicine, Acibadem City Clinic UMHAT Tokuda JSC, under the scientific supervision of Assoc. Prof. Dr. Alexander Ivanov Osichenko, MD.

Dear members of the Scientific Jury,

Worldwide, the number of patients with chronic kidney disease (CKD) is continuously increasing, and this trend is expected to continue in the coming years. CKD is associated with numerous comorbid conditions that significantly reduce quality of life and increase mortality among these patients. Renal bone disease and cardiovascular diseases are among the most common complications of CKD, highlighting the need to explore new diagnostic and therapeutic approaches to manage these conditions. The discovery of Fibroblast Growth Factor 23 (FGF-23) allows clarification of the complex pathogenetic mechanisms involved in maintaining calcium-phosphate homeostasis and their role in the development of renal osteodystrophy, vascular calcification, left ventricular hypertrophy, cognitive impairment, and neurodegenerative disorders in CKD patients. However, routine clinical implementation of FGF-23 and the development of standardized methods for its assessment remain subjects of ongoing research.

In this dissertation, Dr. Nikolova aims to determine the place and role of FGF-23 testing in the diagnostic and therapeutic process for CKD patients, as well as its association with major cardiovascular events, arterial hypertension, and heart failure.

The dissertation submitted for review contains 106 pages and is illustrated with 36 figures and 9 tables. The bibliography includes 129 sources, of which 8 are by Bulgarian authors. The structure fully conforms to the standard dissertation format – introduction, literature review, aim and objectives, materials and methods, results, discussion, conclusions, scientific contributions, literature, publications, and scientific communications. I consider that the proportion of each section is appropriate and consistent with its purpose.

The literature review covers 27 pages, includes 16 chapters, and concludes with findings that clearly define the aim and objectives. The aim is clearly and precisely formulated. The section *Materials and Methods* clearly describes the validated and standardized laboratory and clinical research methods used. A total of 103 patients treated in the Nephrology Department at the Clinic of Internal Medicine, Acibadem City Clinic Tokuda Hospital, over a 2-year period were studied. The number of patients is sufficient to achieve the set objectives. The results are clearly presented over 23 pages. The discussion is thorough and covers 18 pages. All 6 tasks were completed, and the analysis of the results allowed the achievement of

the stated aim. Thirteen conclusions and seven contributions with original and significant scientific potential were made.

The abstract complies with academic requirements and accurately reflects the content of the dissertation.

Contributions with scientific-theoretical and confirmatory value:

- For the first time in Bulgaria, FGF-23 has been studied in CKD patients in pre-dialysis and dialysis stages.
- Data on changes in FGF-23 and PTH levels in CKD stages 3–5 are presented.
- Patients are considered in the context of the new concept of CKD-related mineral and bone disorders and their link to cardiovascular disease.
- The relationship of FGF-23 with phosphate, PTH, and eGFR levels is confirmed.
- The relationship between calcitriol therapy and PTH levels is confirmed, while no association is observed with FGF-23 levels.
- The analysis provides new directions for the diagnosis and treatment of CKD patients.

Dr. Dilyana Nikolova is a nephrology specialist with over 13 years of experience, having previously served 7 years as an assistant at Aleksandrovska Hospital in the Clinic of Nephrology and Transplantology. She holds a specialty in Internal Medicine since 2005. She speaks English and German and has a sufficient number of original publications on the topic, presented at scientific conferences, fulfilling all necessary requirements.

Conclusion:
The submitted dissertation meets all requirements established by the Law on the Development of Academic Staff in the Republic of Bulgaria and its implementing regulations, for obtaining the educational and scientific degree Doctor in the scientific specialty *Internal Medicine*. I recommend that the esteemed members of the Scientific Jury vote positively for awarding Dr. Dilyana Mikhailova Nikolova the degree of Doctor.

Sofia, 12.09.2025

Prepared by: Assoc. Prof. Dr. Daniela Petrova, PhD