

# Treatment Efficacy of PBI-4050, an Orally Active Antifibrotic Agent, Can Be Monitored by Following Urinary Biomarkers in 5/6-Nephrectomized Rats



PROMETIC

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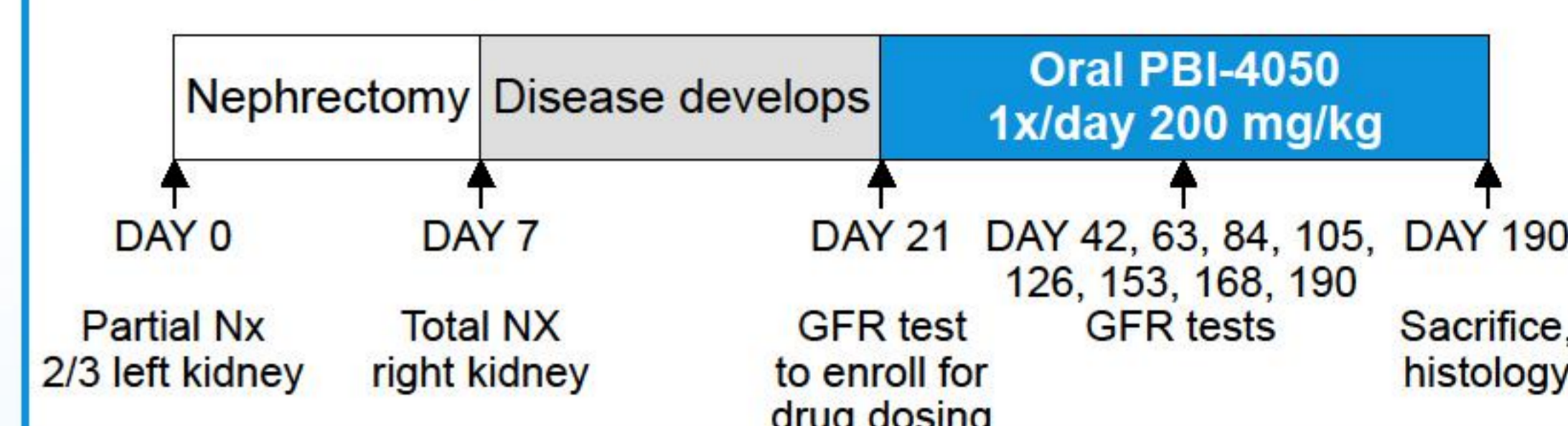
## BACKGROUND AND AIM

PBI-4050, a novel first-in-class orally active compound which is currently in clinical phase Ib/II in Chronic Kidney Disease (CKD) patients, displays antifibrotic activities via a novel mechanism of action. In the present study, we examined the antifibrotic effect of PBI-4050 by evaluating urinary biomarkers in the 5/6-nephrectomized (NX) rats.

## METHODS

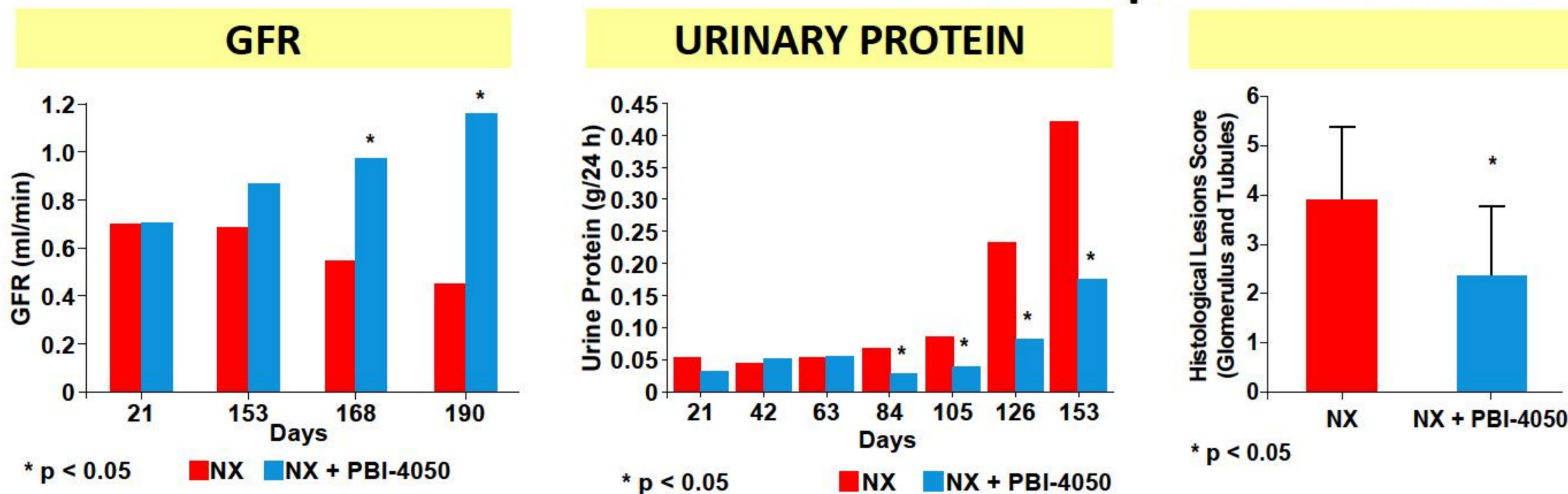
Sprague-Dawley rats were partially nephrectomized (2/3 of the left kidney) on day 0. On day 7 the right kidney was removed. Oral treatment with PBI-4050 (200 mg/kg, once a day) or vehicle was initiated at day 21, following randomization based on glomerular filtration rate (GFR) results. GFR was measured at day 21 and assessed every 3 weeks up to day 190. Urinary markers were analyzed with Bio-Plex Pro™ rat kidney toxicity panels 1 and 2 (Bio-Rad). Statistics: Student's t-test.

### End-stage Renal Disease Model

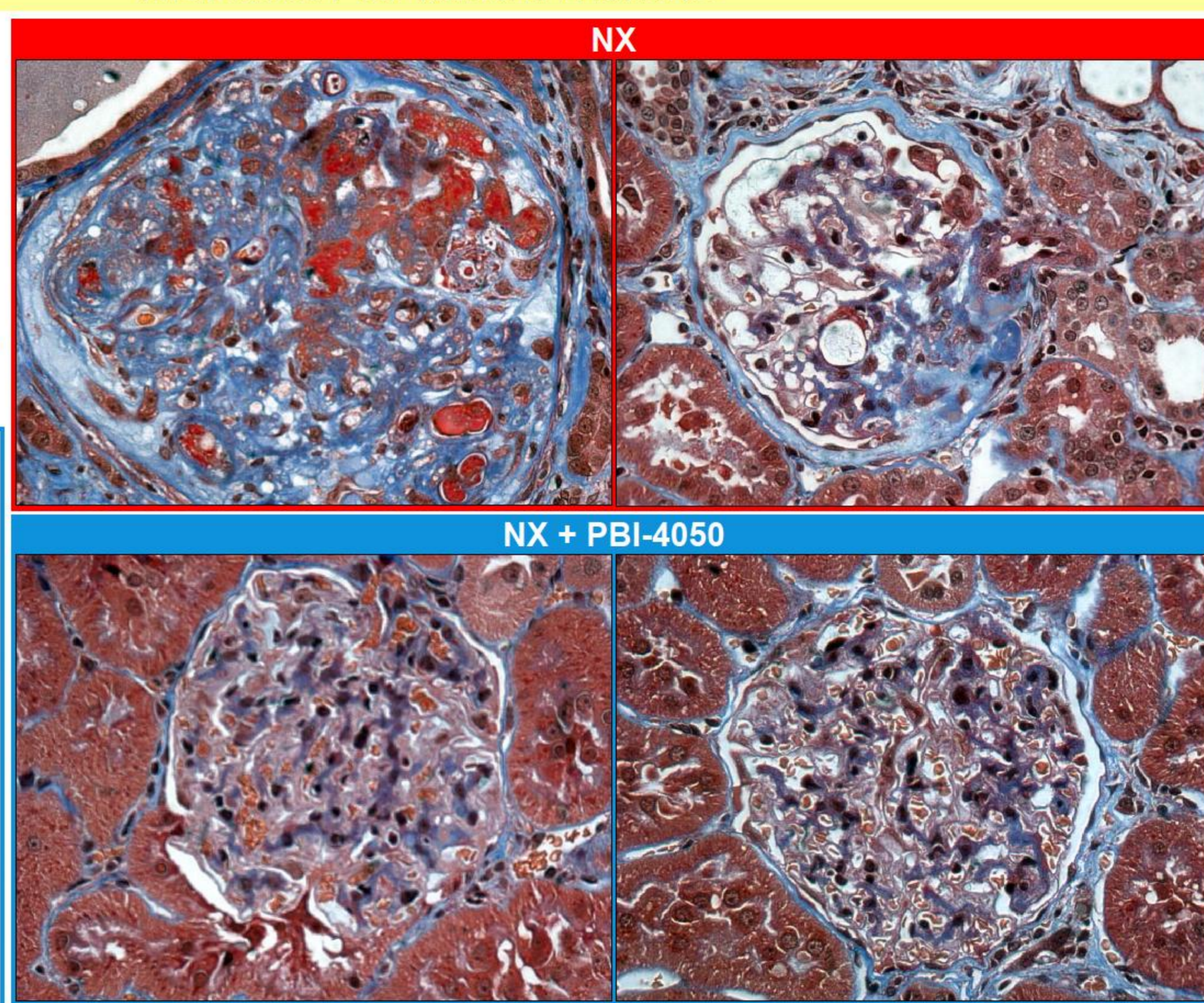


## RESULTS

### PBI-4050 Improves Renal Function and Structure

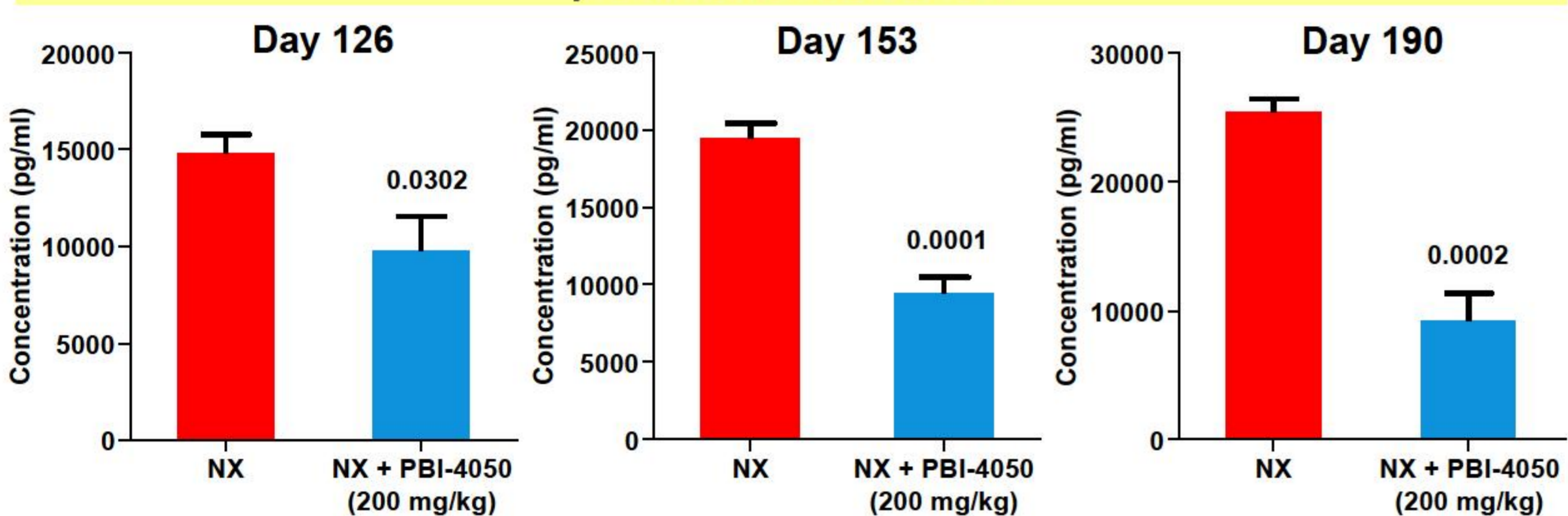


### HISTOLOGY OF KIDNEY LESIONS

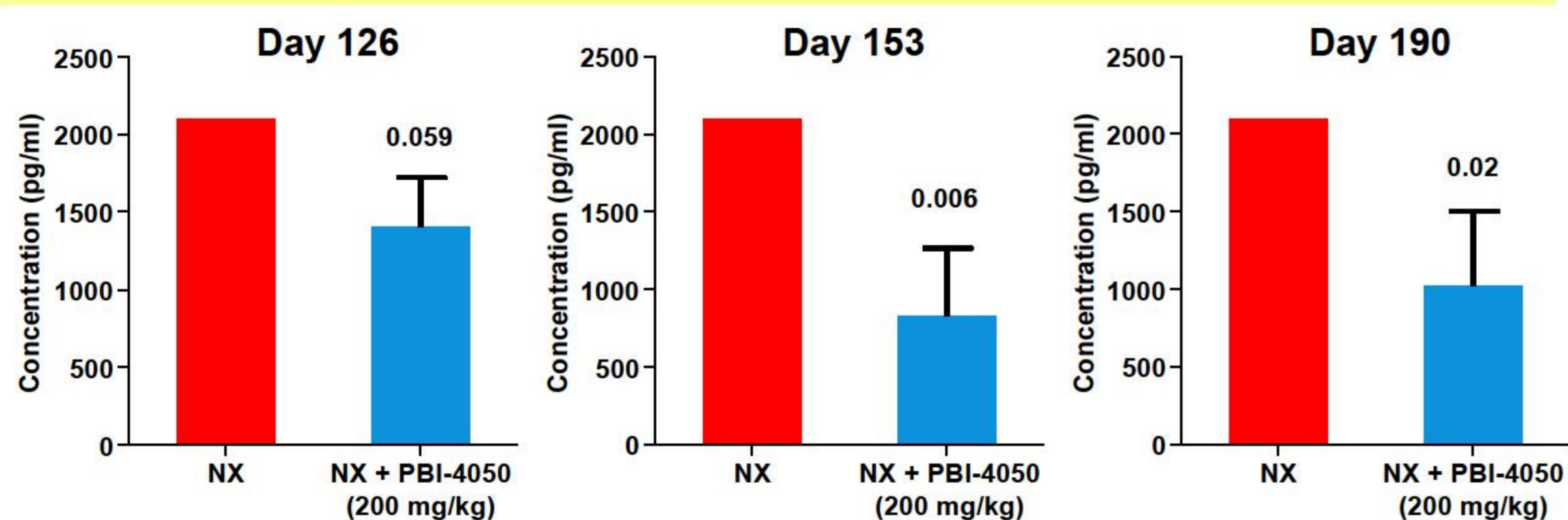


### Urinary Biomarkers in 5/6-NX Rats

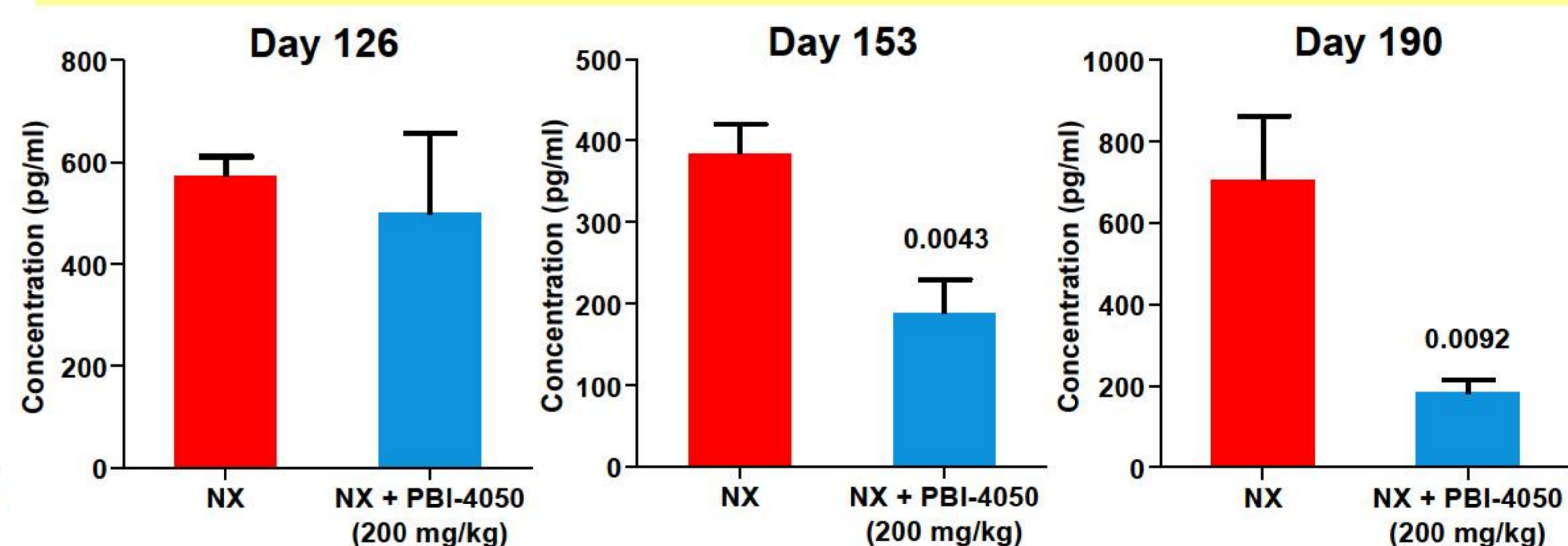
#### β-2-MICROGLOBULIN



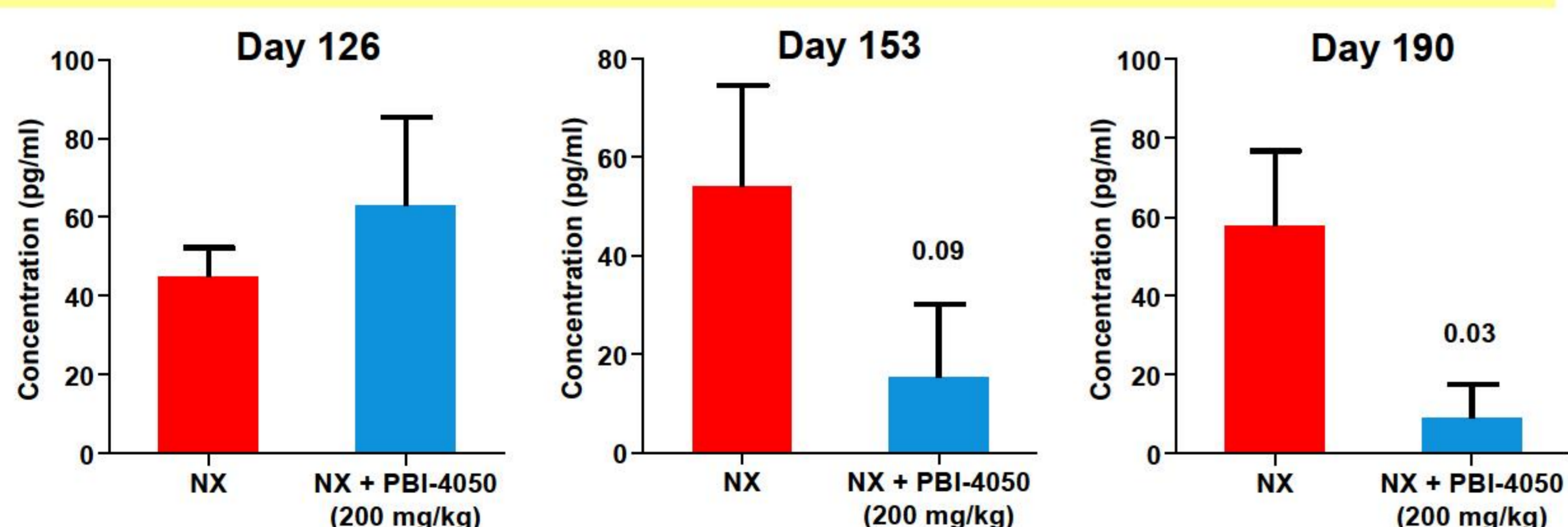
#### CYSTATIN C



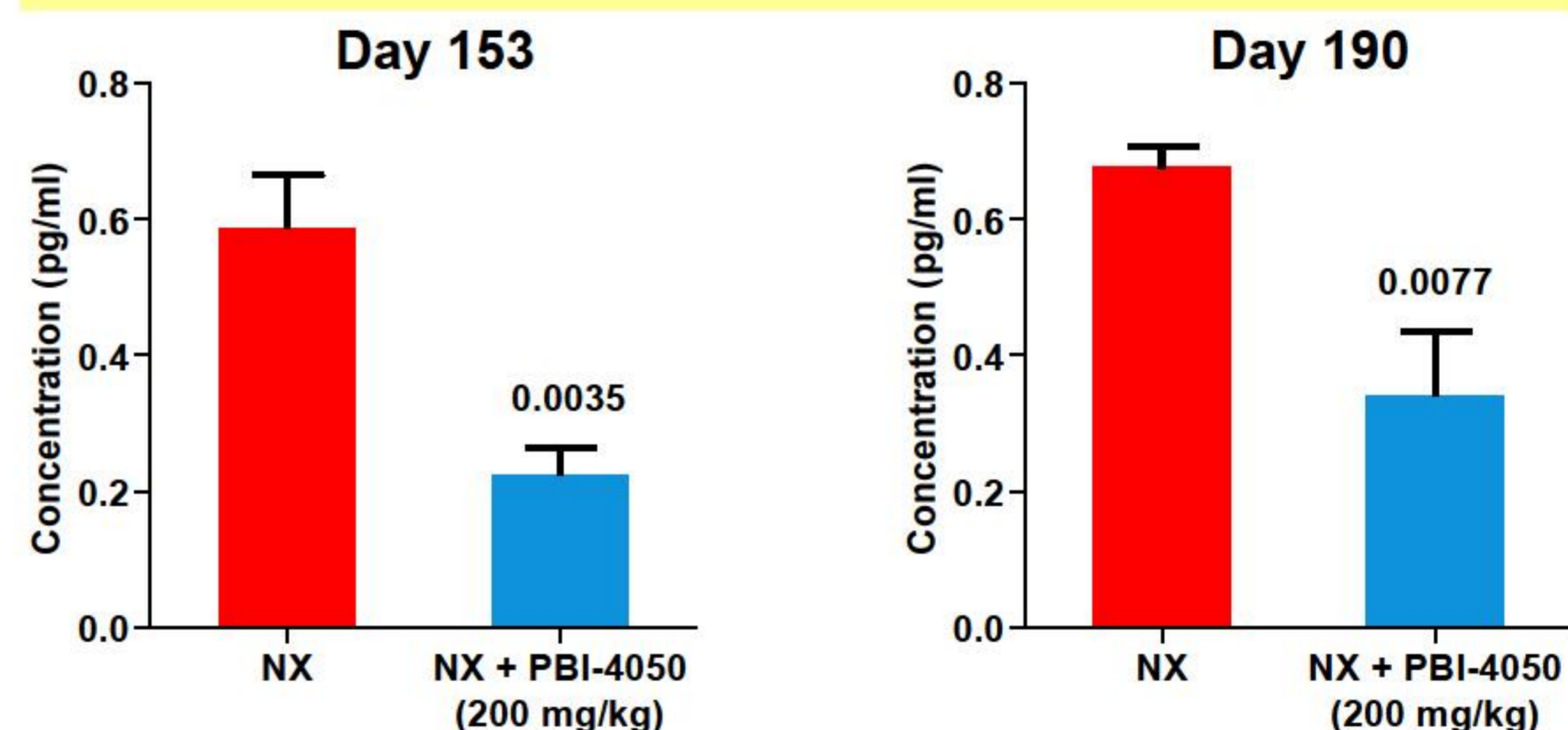
#### CLUSTERIN



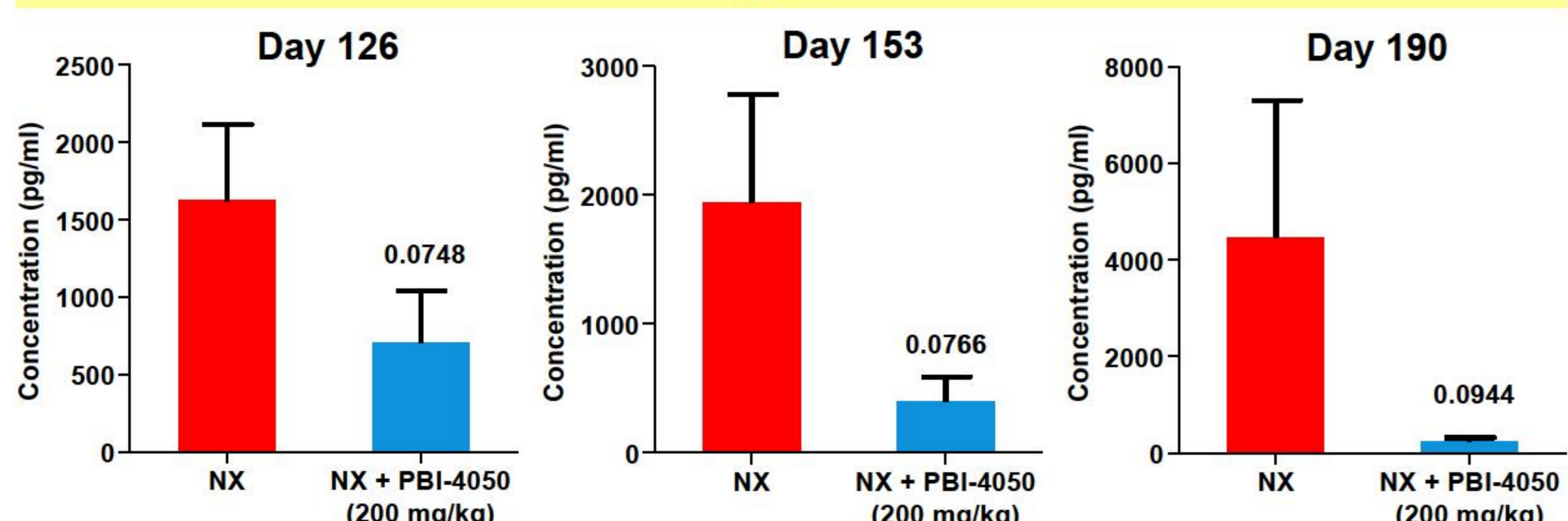
#### CALBINDIN



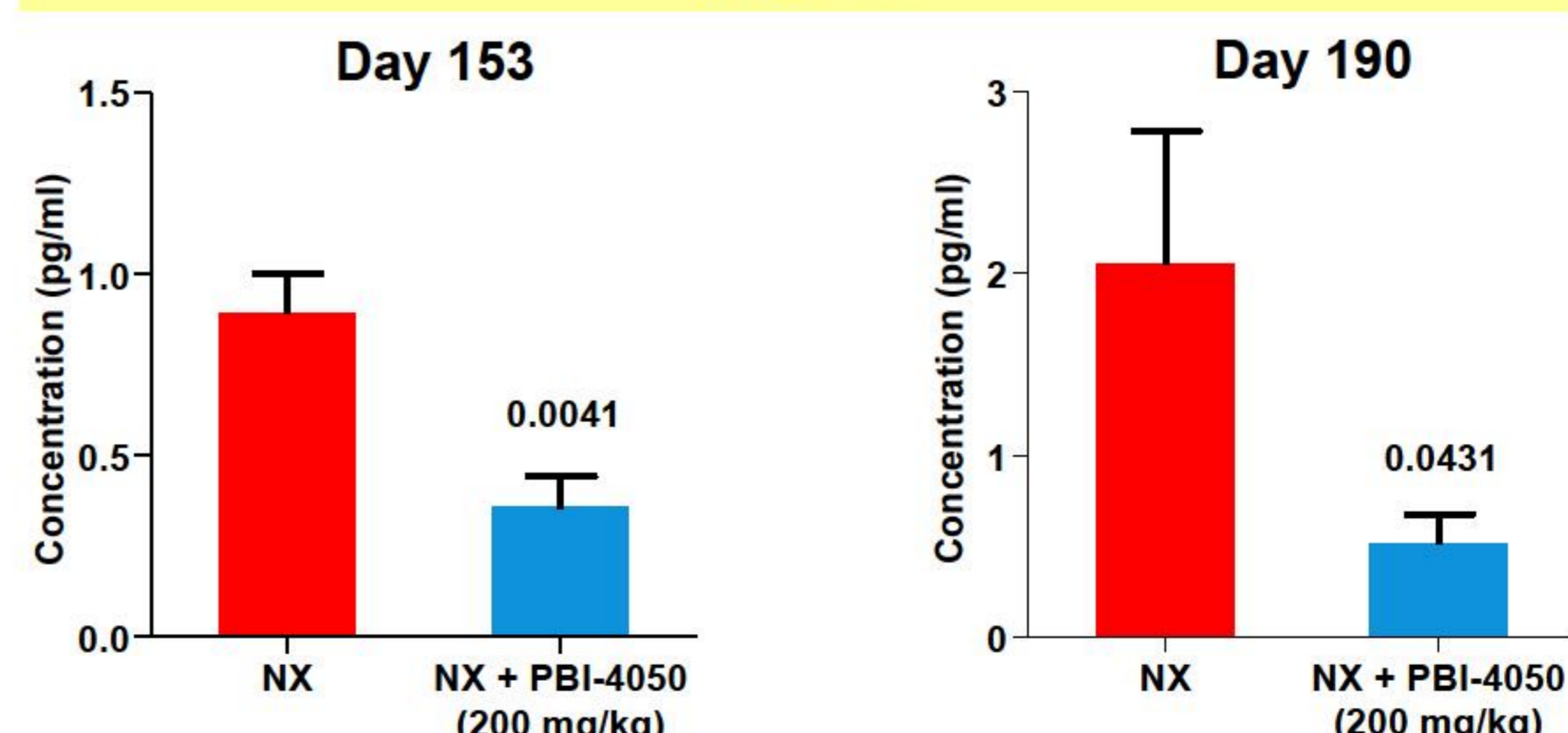
#### KIM-1



#### NGAL



#### MCP-1



## CONCLUSIONS

These results suggest that PBI-4050 offers the potential as a novel therapy for chronic kidney disease by reduction of fibrosis and improvement of kidney function. Treatment efficacy can be monitored with urinary biomarkers.

