

## "ZIRCONIUM-89 (ZR-89) J591 based Positron Emission Tomography (ImmunoPET) as a Basis for Improving Diagnostic Imaging of Prostate Cancer"

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**Abstract:** Standard diagnostic imaging is inadequate in prostate cancer. This fact has complicated individual patient management and delayed development of effective therapies for metastatic disease. We propose a novel solution: <sup>89</sup>Zr-J591 ImmunoPET prostate cancer imaging. Certain facts support the likely success of this approach: 1) PSMA antigen, the target for J591, is expressed nearly ubiquitously on prostate cancer, especially in advanced disease 2) our preliminary studies with Indium-111 J591 detected 93% of known lesions in advanced prostate SPECT but were likely to miss (less sensitive to) deep soft-tissue lesions; 3) PET has greater sensitivity than SPECT for radiotracer detection by 2 orders of magnitude; 4) using directed biopsy of PET-FDG and FDHT positive lesions, the yield of pathologically interpretable samples was >95%. 5) <sup>89</sup>Zr (3-1/2 day T-1/2) has been successfully produced in our cyclotron, and labeled to J591 with high immunoreactivity under cGMP conditions. This revised application includes 3 changes: 1) we narrow our focus to the castrate resistant population, the lethal form of the disease; 2) we propose PET-directed biopsies of individual metastatic lesions in each patient; 3) we add Broad Institute investigators to obtain their expertise in analysis of biopsy specimens for heterogeneity of metabolome genomics, signaling, protein expression (esp AR and PSMA), and sequencing of key proteins (ie AR). These analyses will validate <sup>89</sup>Zr-J591 ImmunoPET and may provide insight into the biology of prostate cancer imaging, including an explanation for the variable pattern of lesion detection observed with metabolically based PET imaging of prostate cancer.