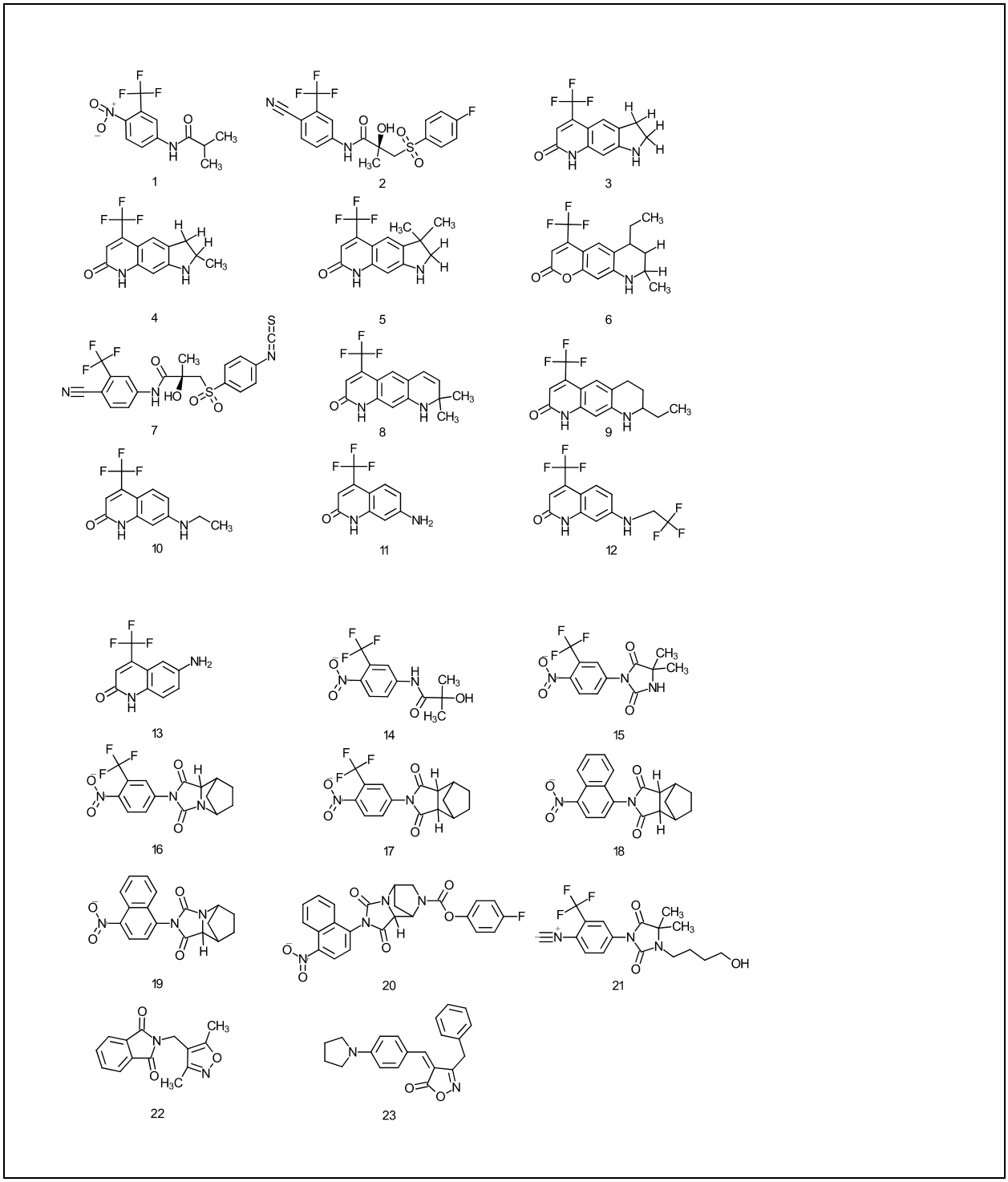
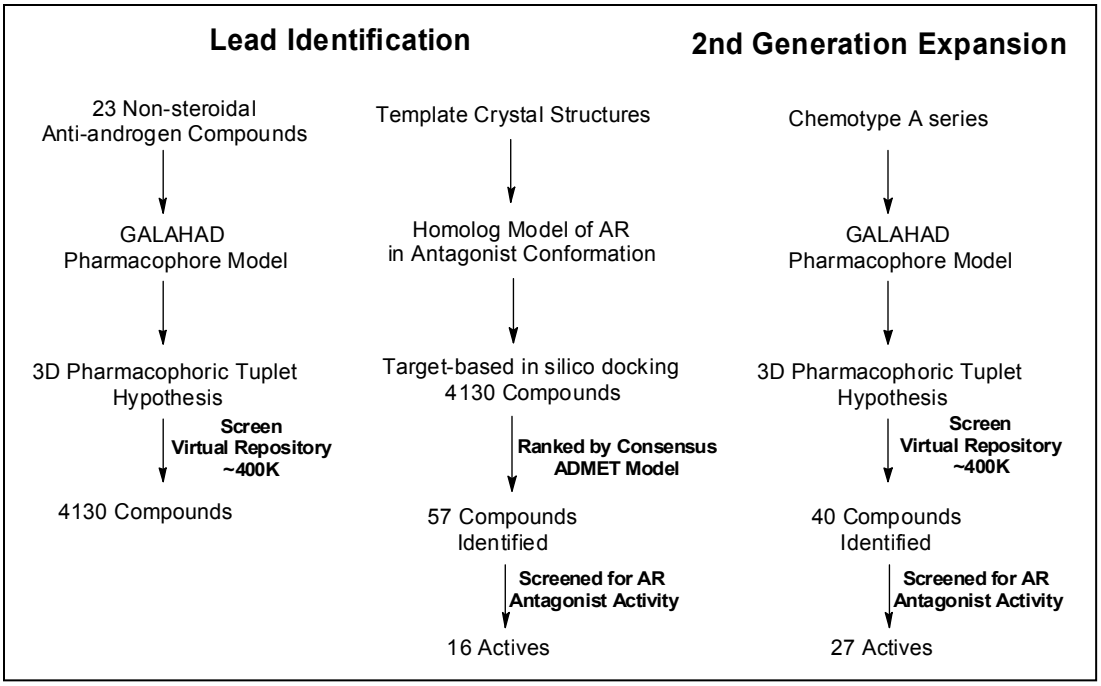
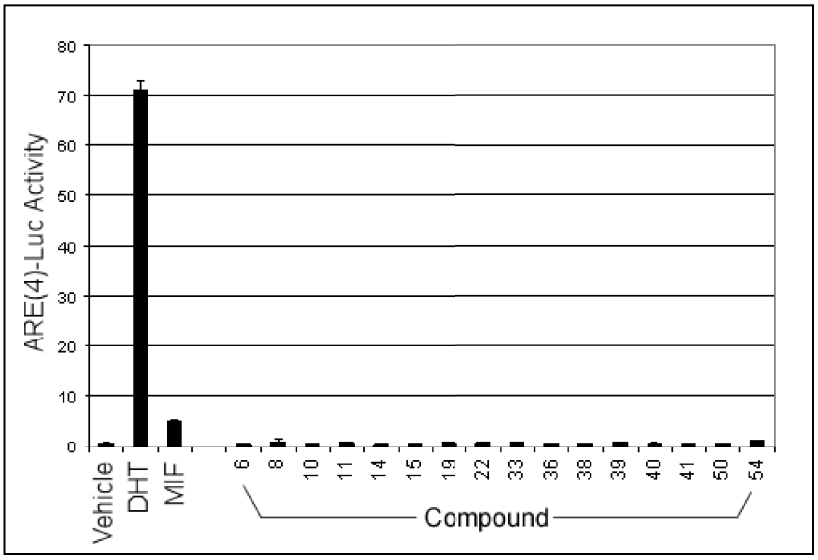


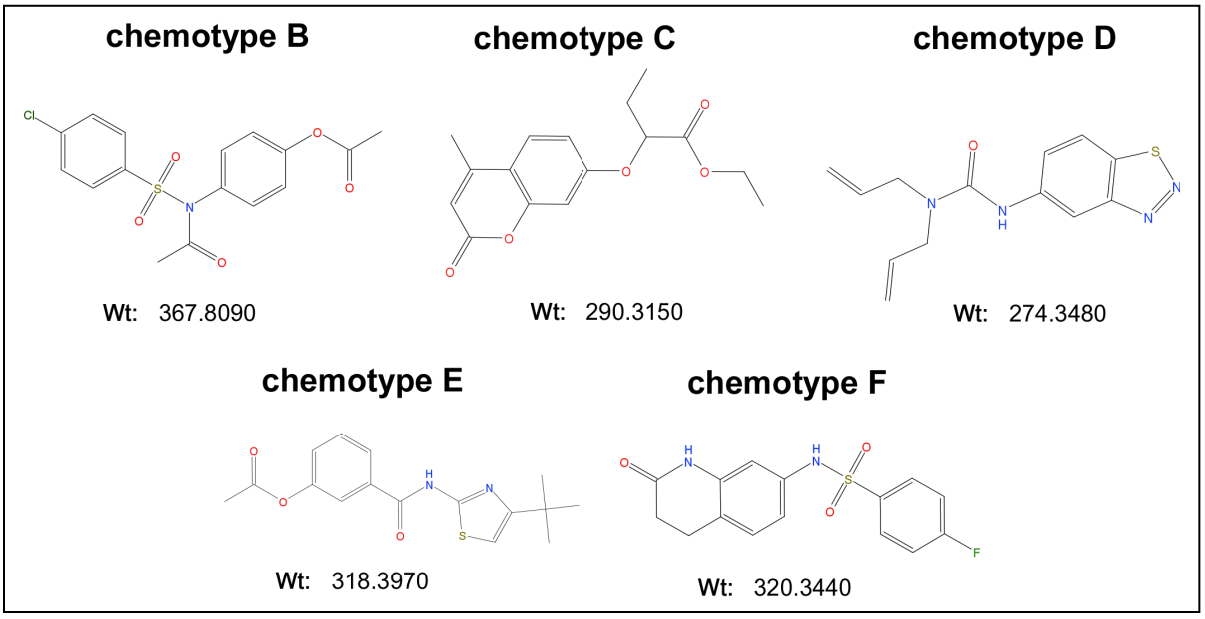
Supplemental Figure 1. Non-steroidal anti-androgens used for the active pharmacophoric fingerprint.



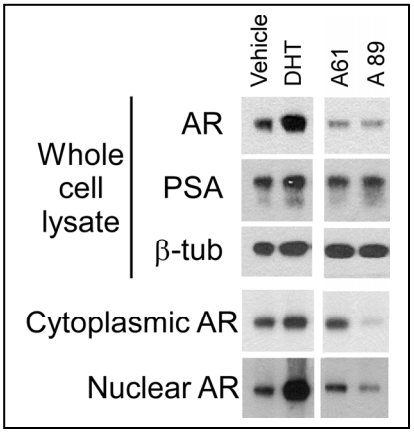
Supplemental Figure 2. Flow chart for *in silico* discovery of AR antagonists and lead expansion.



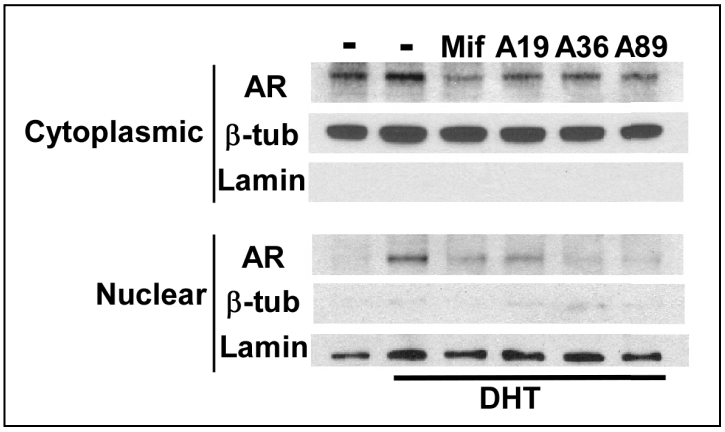
Supplemental Figure 3. AR antagonists in the absence DHT do not have agonist activity. Luciferase activity from COS7 cells transfected with AR and AR-responsive luciferase reporter plasmids followed by drug treatment with the indicated compounds for 24 hours. DHT (10 nM), Mifepristone (Mif, 100 nM), or the 16 selected compounds (50 μM).



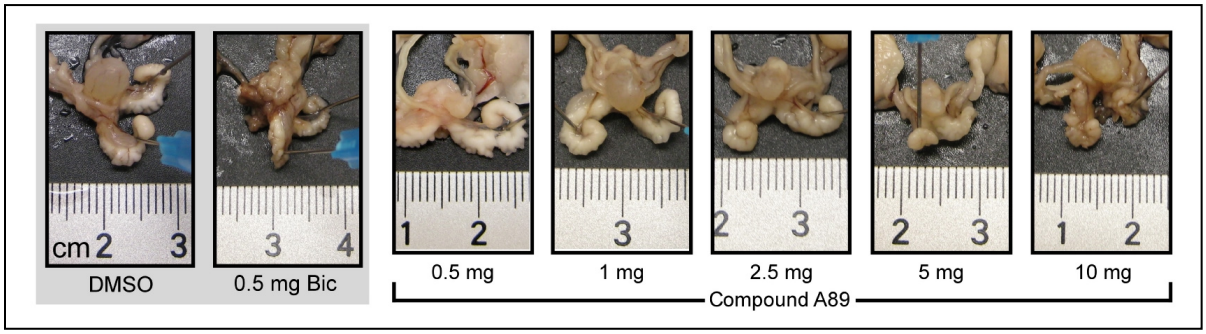
Supplemental Figure 4. Structures of chemotypes B-F AR antagonists.



Supplemental Figure 5. Chemotype A compounds do not stimulate PSA synthesis or nuclear translocation of AR in C4-2 cells. C4-2 cells in steroid depleted medium (RPMI-1640 with 5% charcoal-dextran stripped serum) were stimulated for 4 hours with vehicle, 10 nM DHT, or 10 μM A61 or A81.



Supplemental Figure 6. Chemotype A compounds impair DHT stimulated nuclear localization of AR. C4-2 cells cultured fo r3 days in steroid depleted medium (RPMI-1640 with 5% charcoal-dextran stripped serum) were treated as indicated for 24 hours with DHT (10 nM) and mifipristone (Mif) or chemotype A compounds (10 μM). Equal amounts of total cytoplasmic or nuclear protein extracts were then immunoblotted as indicated.



Supplemental Figure 7. AR antagonist activity of A89 *in vivo*. Male mice were treated with daily intraperitoneal injections of vehicle (DMSO), 0.5 mg bicalutamide (Bic), or A89 at 0.5, 1, 2.5, 5, or 10 mg. Mice were sacrificed after 7 days and seminal vesicle involution was assessed as a marker of AR antagonist activity.