SUPPLEMENTARY APPENDIX

Table S1. Pharmacokinetic Parameters

Table 3 Pharmacokinetic Parameters								
SUBJ ID	**Cmax (ug/mL)**	**AUCall dose1 (day*ug/mL)**	**AUCINF dose1 (day*ug/mL)**	**AUCall dose 1,2 (day*ug/mL)**	**CLss (mL/day)**	**Accumulation Index**	**T1/2 (day)**	**r^2**
101-02	464	3397	6500	24431	295	1.92	13.2	0.893
102-02	215	1772	3051	3701	566	1.73	11.3	0.967
103-02	331	2620	4543	2696	383	1.75	11.4	0.943
104-02	297	2065	3432	7830	462	1.59	9.8	0.913
105-01	387	2391	4142	10409	417	1.73	11.3	0.807
107-01	633	3066	5675	11055	313	1.85	12.5	0.684
108-02	480	3908	6961	11253	256	1.76	11.6	0.427
109-02	362	2101	4099	10834	475	1.91	13.1	0.915
110-01	506	3760	5428	18081	266	1.45	8.3	0.979
111-02	449	3121	4360	12876	321	1.41	7.8	0.976
112-02*	397	2611	9514	10360	382	3.09	24.9	0.180
113-02	726	3818	8481	16150	262	2.27	16.7	0.669
N	**12**	**12**	**11**	**12**	**11**	**11**	**11**	**11**
Mean	**437**	**2886**	**5515**	**11640**	**365**	**1.761**	**11.5**	**0.834**
SD	**141**	**735**	**2010**	**5945**	**103**	**0.240**	**2.5**	**0.174**
Median	**423**	**2843**	**4986**	**10945**	**321**	**1.746**	**11.4**	**0.913**

*Terminal phase parameters could not be calculated (Regression RSQ < 0.2). Individual estimates reported but not included in means

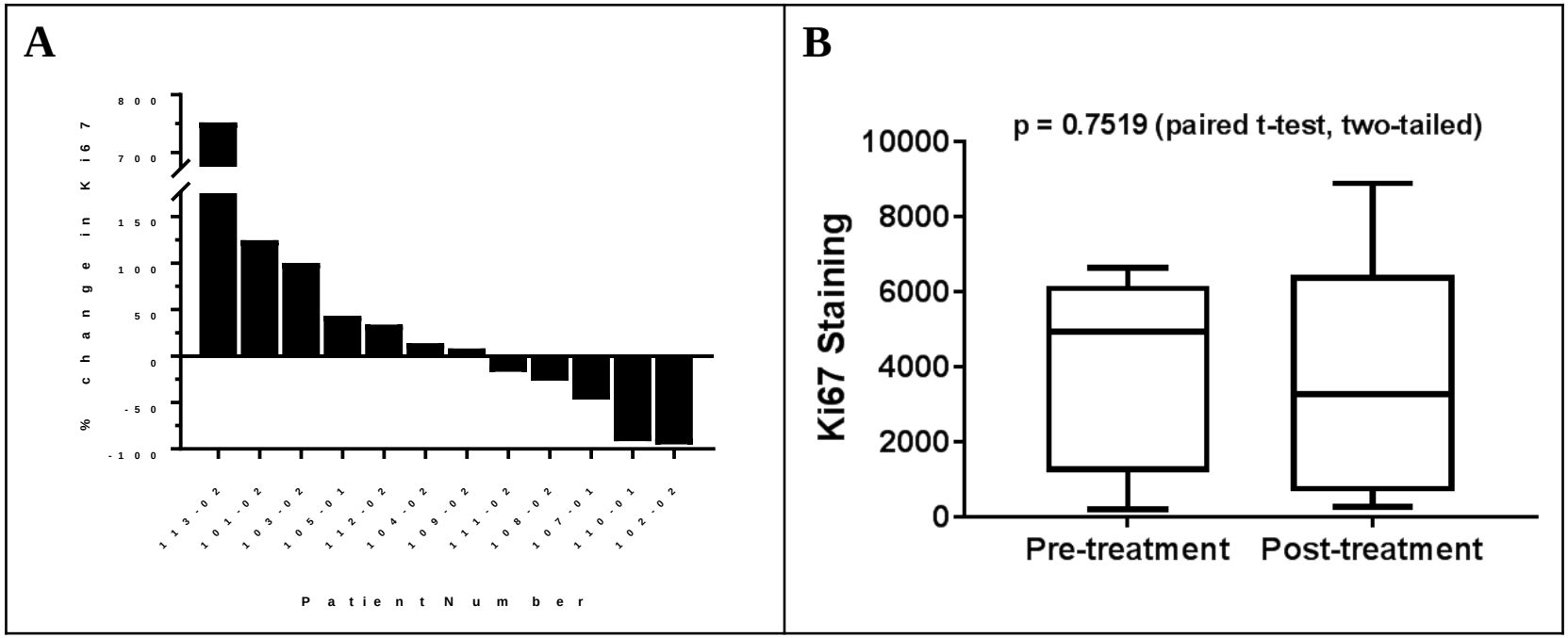


Figure S1. Ki67 Expression by IHC. (A) Change in Ki67 level in individual patient tumor samples and (B) mean Ki67 levels for all tumor samples (n=12) before and after CDX-3379 treatment.

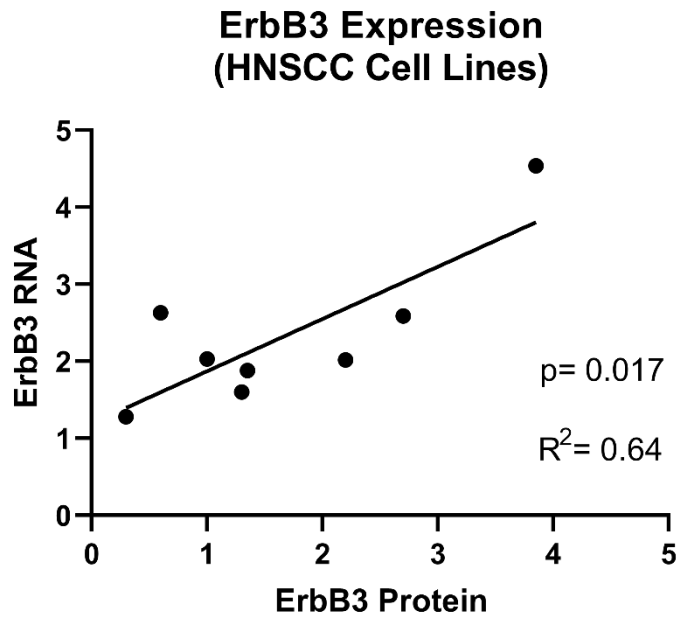
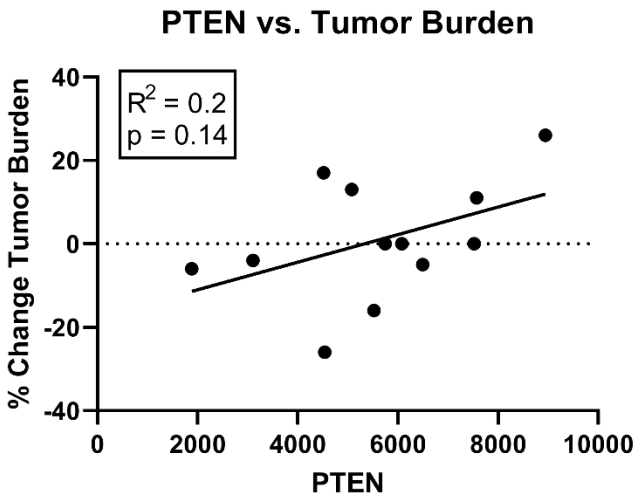
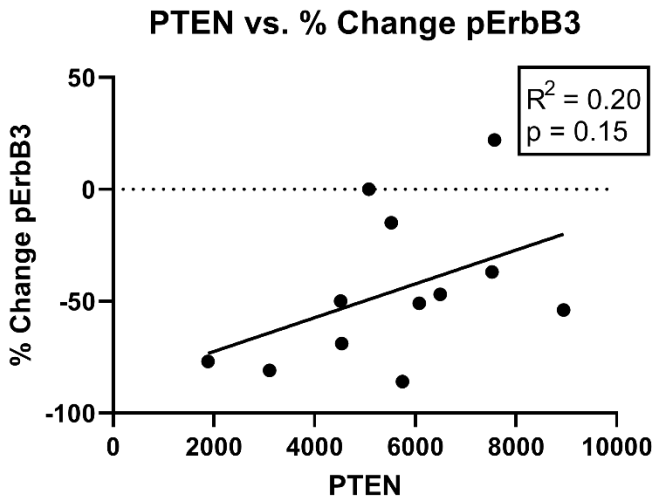
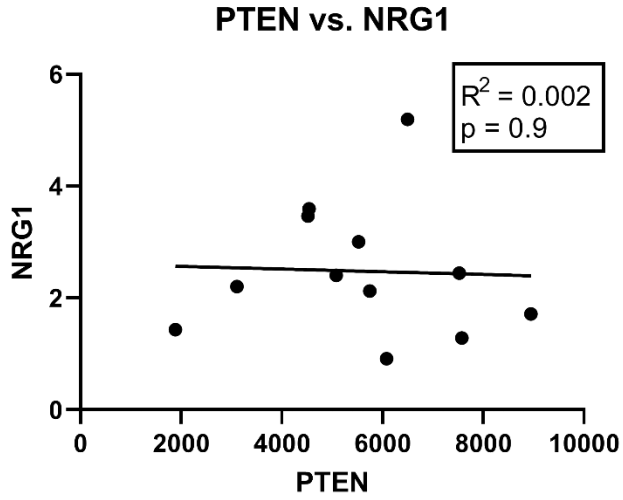
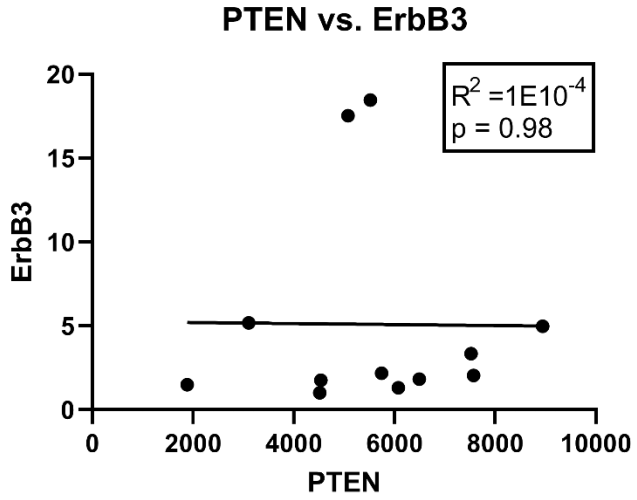


Figure S2: ErbB3 RNA and protein expression are significantly correlated. ErbB3 RNA and total protein were evaluated in a panel of 8 HNSCC cell lines. Linear correlation analysis reveals the two variables are significantly associated. The correlation was performed by linear regression (GraphPad Prism 7.02).

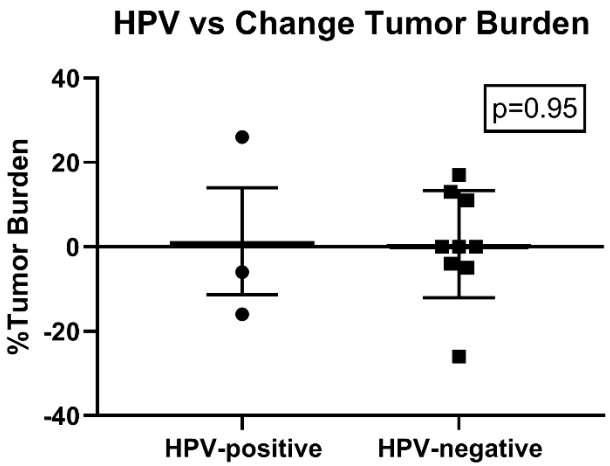

PTEN vs. Tumor Burden
% Change Tumor Burden
PTEN
R2 = 0.2
p = 0.14
40
20
0
-20
-40
0
2000
4000
6000
8000
10000

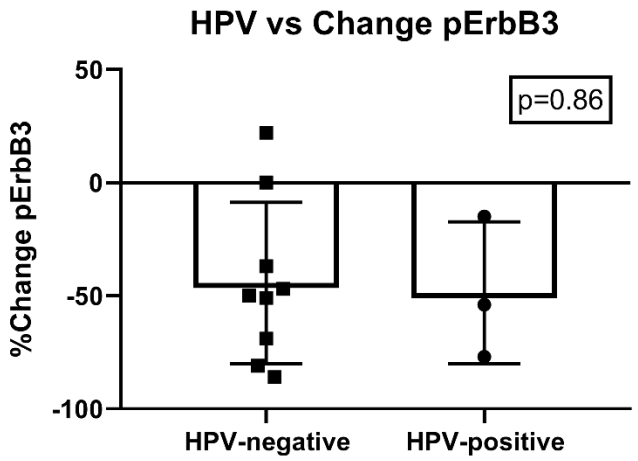

PTEN vs. % Change pErbB3
% Change pErbB3
PTEN
R2 = 0.20
p = 0.15
50
0
-50
-100
0
2000
4000
6000
8000
10000

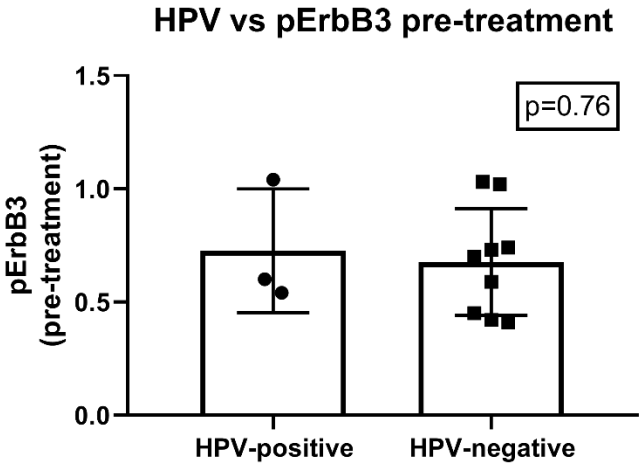

PTEN vs. NRG1
NRG1
PTEN
R2 = 0.002
p = 0.9
6
4
2
0
0
2000
4000
6000
8000
10000

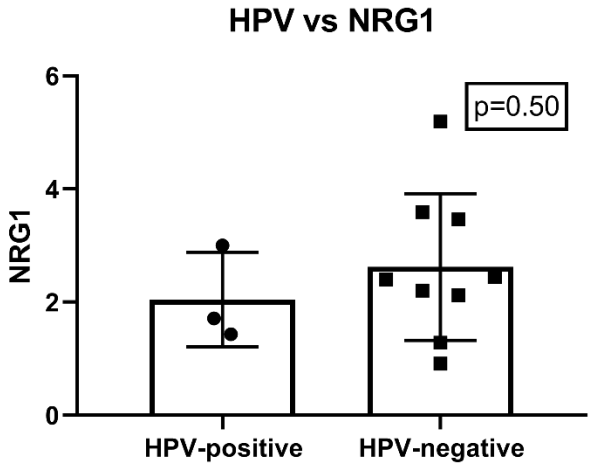

PTEN vs. ErbB3
ErbB3
PTEN
R2 =1E10-4
p = 0.98
20
15
10
5
0
0
2000
4000
6000
8000
10000

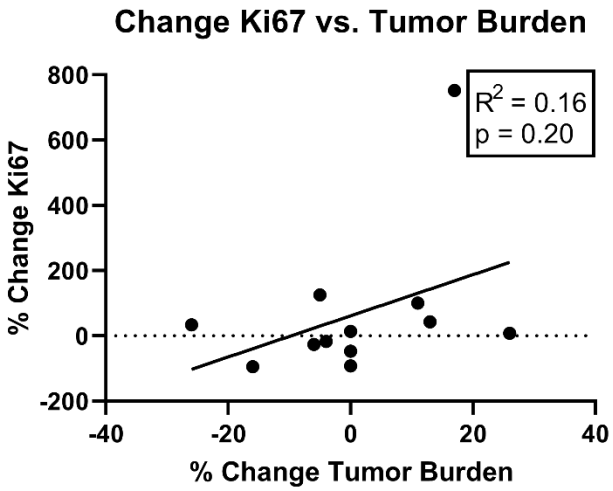
.

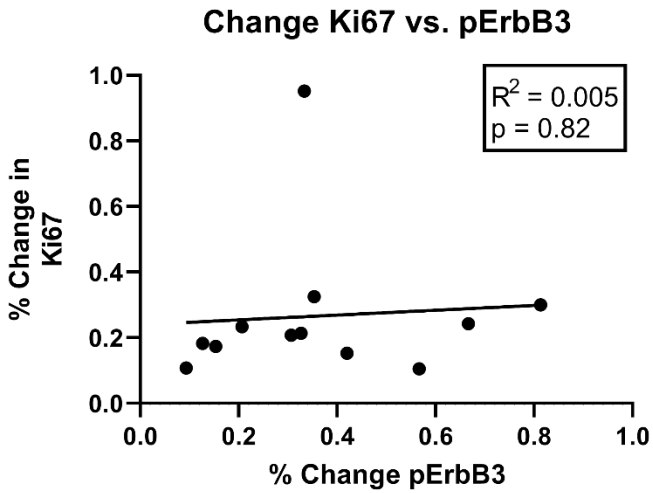

HPV vs Change Tumor Burden
%Tumor Burden
40
20
0
-20
-40
p=0.95
HPV-positive
HPV-negative

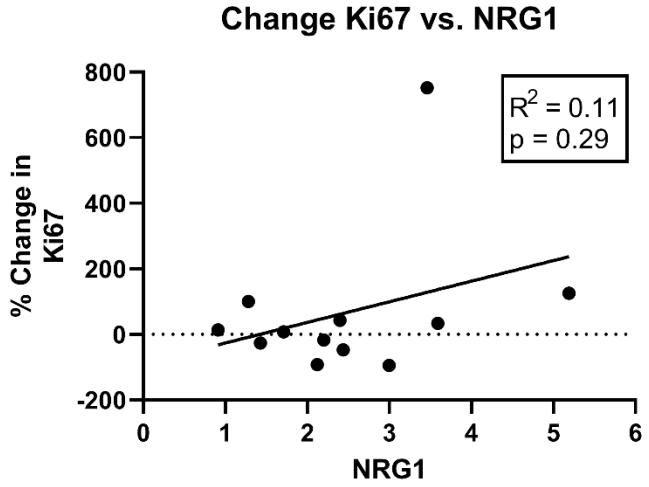

HPV vs Change pErbB3
%Change pErbB3
50
0
-50
-100
p=0.86
HPV-negative
HPV-positive

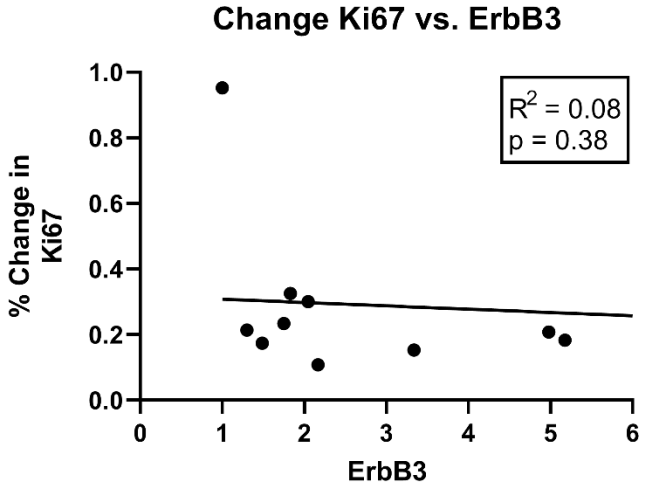

HPV vs pErbB3 pre-treatment
pErbB3
(pre-treatment)
1.5
1.0
0.5
0.0
p=0.76
HPV-positive
HPV-negative

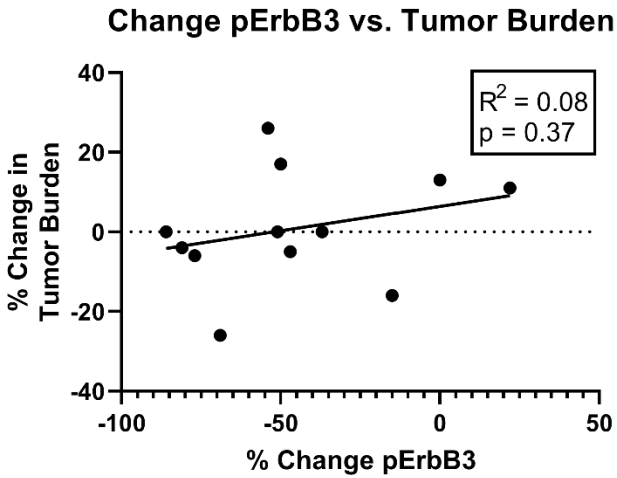

HPV vs NRG1
NRG1
6
4
2
0
p=0.50
HPV-positive
HPV-negative

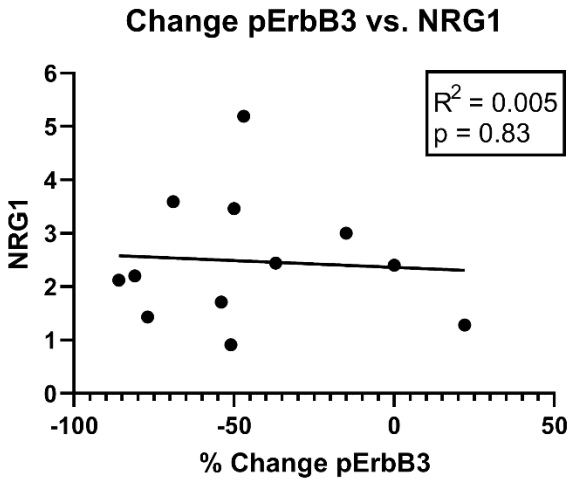

Change Ki67 vs. Tumor Burden
R^2 = 0.16
p = 0.20
% Change Ki67
% Change Tumor Burden
800
600
400
200
0
-200
-40
-20
0
20
40


Change Ki67 vs. pErbB3
R^2 = 0.005
p = 0.82
% Change in Ki67
% Change pErbB3
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.2
0.4
0.6
0.8
1.0


Change Ki67 vs. NRG1
R^2 = 0.11
p = 0.29
% Change in Ki67
NRG1
800
600
400
200
0
-200
0
1
2
3
4
5
6


Change Ki67 vs. ErbB3
R^2 = 0.08
p = 0.38
% Change in Ki67
ErbB3
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
6


Change pErbB3 vs. Tumor Burden
R^2 = 0.08
p = 0.37
% Change in Tumor Burden
% Change pErbB3
40
20
0
-20
-40
-100
-50
0
50


Change pErbB3 vs. NRG1
R^2 = 0.005
p = 0.83
NRG1
% Change pErbB3
6
5
4
3
2
1
0
-100
-50
0
50

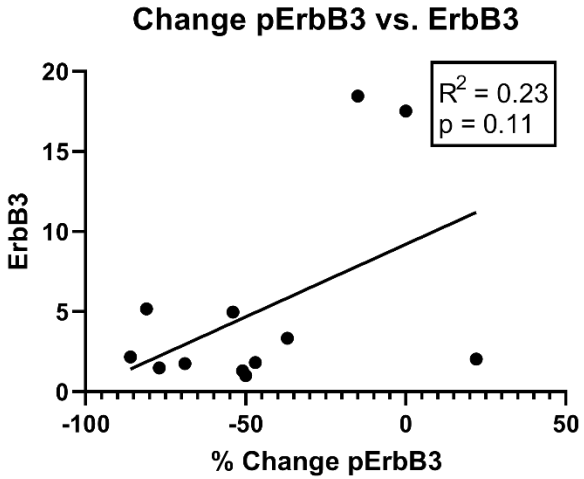

Change pErbB3 vs. ErbB3
R^2 = 0.23
p = 0.11
ErbB3
% Change pErbB3
20
15
10
5
0
-100
-50
0
50

Figure S3. Statistical correlations between biomarker subsets. Correlations were performed by linear regression and p-values were calculated by unpaired, two-tailed t-tests (GraphPad Prism 7.02). Tumor burden represents percent change from baseline in the sum of longest diameters of target lesion(s) for each study patient. Change in Ki67 represents the percent change in Ki67 level by IHC (AQUA®) from baseline after CDX-3379 treatment in individual patient tumor samples. NRG1, NRG2, ErbB3, and PTEN assessed using post-treatment tumor resection samples for all patients except 102-02, 103-02, and 104-02 (pre-treatment biopsies were evaluated). mRNA expression levels of NRG1, andErbB3 were determined by quantitative RNAScope® assays. mRNA expression levels were calculated as previously described (Alvarado, D., et al., ErbB activation signatures as potential biomarkers for anti-ErbB3 treatment in HNSCC. PLoS One, 2017. 12(7): p. e0181356; Bordeaux, J.M., et al., Quantitative in situ measurement of estrogen receptor mRNA predicts response to tamoxifen. PLoS One, 2012. 7(5): p. e36559). PTEN expression was assessed by IHC (AQUA®).