**Supplementary Figure 1.** Analytical pipeline for conducting mediation analyses in an exposure mixtures framework. Schematic depicts shrinkage of the exposure matrix into low and high molecular weight phthalate ERS, followed by causal mediation analyses utilizing ERS, hormone mediators, and birth outcomes.
Supplementary Figure 2. Causal diagrams for mediation analyses in the counterfactual framework with a) exposures at visit 1 ($A_1$) and mediators at visit 1 ($M_1$), b) the average of exposures at visits 1 and 2 ($\bar{A}_2$) and mediators at visit 3 ($M_3$), and c) the average of exposures at all 3 visits ($\bar{A}_3$) and mediators at visit 3 ($M_3$), with confounders (C) and outcomes (Y) that do not vary with time.
Supplementary Figure 3. Weights assigned from ridge regression, stratified by fetal sex, depicting the relative importance of each phthalate metabolite for predicting birth outcomes at each study visit.
Supplementary Figure 4. Scatter plot of natural indirect effects (NIE) on the x-axis and their $-\log_{10}(p$ values) on the y-axis, for three main mediation models, for all combinations of three covariates (maternal age, maternal education, and fetal sex). The horizontal dashed line represents a p-value of 0.05; covariate combinations giving an NIE p-value < 0.05 fall above the dashed line.
**Supplementary Figure 5.** Estimated $-\log_{10}(p$-values) of mediating effects by hormone concentrations on the associations between phthalate ERS and birth outcomes, among mothers carrying a male fetus.

From left to right within each chart, the vertical dashed lines represent $p$-values of 0.1, 0.05, and 0.01. All models were adjusted for continuous maternal age and categorical education.
**Supplementary Table 1.** Maternal demographic and birth characteristics of 1011 Puerto Rican mothers.

|                               | Median (IQR) | Erskine R. Shipley Population | Mediation Population* |
|-------------------------------|--------------|-------------------------------|-----------------------|
| **Gestational Age at Delivery (weeks)** |              | 39.3 (1.79)                  | 39.3 (1.86)           |

| **N (%)** | Erskine R. Shipley Population | Mediation Population* |
|-----------|-------------------------------|-----------------------|
| **Preterm Birth** |                                |                       |
| Yes       | 89 (8.8%)                     | 65 (9.2%)             |
| No        | 911 (90.1%)                   | 632 (89.6%)           |
| Missing   | 11 (1.1%)                     | 8 (1.1%)              |
| **Spontaneous PTB** |                                |                       |
| Yes       | 52 (5.1%)                     | 39 (5.5%)             |
| No        | 921 (91.1%)                   | 640 (90.8%)           |
| Missing   | 38 (3.8%)                     | 26 (3.7%)             |
| **Maternal Age (years)** |                                |                       |
| 18-24     | 357 (35.3%)                   | 247 (35.0%)           |
| 25-29     | 309 (30.6%)                   | 215 (30.5%)           |
| 30-34     | 214 (21.2%)                   | 150 (21.3%)           |
| 35-41     | 131 (13.0%)                   | 93 (13.2%)            |
| Missing   | 0 (0.0%)                      | 0 (0.0%)              |
| **Maternal Education** |                                |                       |
| GED or less | 195 (19.3%)                   | 147 (20.9%)           |
| Some College | 337 (33.3%)                   | 236 (33.5%)           |
| Bachelors or Higher | 479 (47.4%)                   | 322 (45.7%)           |
| Missing   | 0 (0.0%)                      | 0 (0.0%)              |
| **Employment Status** |                                |                       |
| No        | 344 (34.0%)                   | 243 (34.5%)           |
| Yes       | 662 (65.5%)                   | 458 (65.0%)           |
| Missing   | 5 (0.5%)                      | 4 (0.6%)              |
| **Annual Household Income** |                                |                       |
| <10k      | 255 (25.2%)                   | 195 (27.7%)           |
| 10k-<30k  | 293 (29.0%)                   | 196 (27.8%)           |
| 30k-<50k  | 223 (22.1%)                   | 157 (22.3%)           |
| >=50k     | 126 (12.5%)                   | 77 (10.9%)            |
| Missing   | 114 (11.3%)                   | 80 (11.3%)            |
| **Marital Status** |                                |                       |
| Single    | 168 (16.6%)                   | 128 (18.2%)           |
| Married   | 553 (54.7%)                   | 371 (52.6%)           |
| Cohabitating | 286 (28.3%)                   | 202 (28.7%)           |
| Missing   | 4 (0.4%)                      | 4 (0.6%)              |
| **Smoking Status** |                                |                       |
| Never     | 873 (86.4%)                   | 611 (86.7%)           |
|                        | Subset 1 | Subset 2 |
|------------------------|----------|----------|
| Ever                   | 118 (11.7%) | 80 (11.3%) |
| Current                | 17 (1.7%) | 12 (1.7%) |
| Missing                | 3 (0.3%) | 2 (0.3%) |

**Daily Environmental Tobacco Smoke Exposure**

|                      | Subset 1 | Subset 2 |
|----------------------|----------|----------|
| Never                | 848 (83.9%) | 590 (83.7%) |
| 1 Hour or less       | 37 (3.7%) | 21 (3.0%) |
| >1 Hour              | 42 (4.2%) | 35 (5.0%) |
| Missing              | 84 (8.3%) | 59 (8.4%) |

**Alcohol Use**

|                      | Subset 1 | Subset 2 |
|----------------------|----------|----------|
| Never                | 520 (51.4%) | 358 (50.8%) |
| Yes, before Pregnancy| 429 (42.4%) | 303 (43.0%) |
| Yes, currently       | 58 (5.7%) | 42 (6.0%) |
| Missing              | 4 (0.4%) | 2 (0.3%) |

**Number of Previous Children**

|         | Subset 1 | Subset 2 |
|---------|----------|----------|
| 0       | 327 (32.3%) | 233 (33.0%) |
| 1       | 375 (37.1%) | 260 (36.9%) |
| 2 to 5  | 117 (11.6%) | 73 (10.4%) |
| Missing | 192 (19.0%) | 139 (19.7%) |

**Pre-Pregnancy BMI**

|              | Subset 1 | Subset 2 |
|--------------|----------|----------|
| [0, 25]      | 515 (50.9%) | 360 (51.1%) |
| (25, 30]     | 269 (26.6%) | 177 (25.1%) |
| Above 30     | 178 (17.6%) | 128 (18.2%) |
| Missing      | 49 (4.8%) | 40 (5.7%) |

**Fetal Sex**

|        | Subset 1 | Subset 2 |
|--------|----------|----------|
| Female | 462 (45.7%) | 331 (47.0%) |
| Male   | 540 (53.4%) | 369 (52.3%) |
| Missing| 9 (0.9%) | 5 (0.7%) |

*Subset includes all women with mediator data (N=705).*
**Supplementary Table 2.** Results from the *medsens* sensitivity analysis showing the range of $\rho$ values for which the confidence interval of the natural indirect effect contains zero.

| Exposure            | Mediator  | Outcome       | $\rho$ Sensitivity Range |
|---------------------|-----------|---------------|--------------------------|
| Visit 1 HMW ERS     | Visit 1 fT4 | Spont. PTB   | 0.1 – 0.2                |
| Visit 1 HMW ERS     | Visit 1 fT4 | Gest. Age at Birth | -0.2 – 0                |
| Visit 1 LMW ERS     | Visit 1 fT4 | Spont. PTB   | -0.9 – 0.9               |
| Visit 1 LMW ERS     | Visit 1 Test. | Spont. PTB | -0.2 – 0                |
| Visit 2 HMW ERS     | Visit 3 Prog. | Spont. PTB | 0.1 – 0.3               |
| Visit 3 HMW ERS     | Visit 3 Prog. | Spont. PTB | 0.1 – 0.3               |
Supplementary Table 3. Natural indirect effect estimates and percent mediated with an interquartile range increase in low or high molecular weight phthalate ERS over the study period, among mothers carrying a male fetus.

| Low Molecular Weight ERS | Mediator | Outcome | NIE (95% CI) | Percent Mediateda | NIE (95% CI) | Percent Mediateda | NIE (95% CI) | Percent Mediateda |
|-------------------------|----------|---------|--------------|-------------------|--------------|-------------------|--------------|-------------------|
| PTB CRH                 |          | 0.000 (-0.006, 0.007) | 0.70% | 0.005 (-0.002, 0.017) | 8.04% | 0.005 (-0.002, 0.017) | 9.84% |
| PTB Estriol              |          | 0.003 (-0.008, 0.015) | 7.99% | -0.002 (-0.008, 0.003) | NA | -0.003 (-0.015, 0.005) | NA |
| PTB Prog.               |          | 0.006 (-0.005, 0.019) | 15.0% | 0.001 (-0.005, 0.010) | 1.87% | 0.002 (-0.003, 0.011) | 1.66% |
| PTB Prog/E3             |          | 0.000 (-0.004, 0.004) | 0.00% | 0.003 (-0.002, 0.013) | 4.58% | -0.002 (-0.011, 0.005) | NA |
| PTB Test.               |          | 0.000 (-0.007, 0.006) | NA | 0.002 (-0.004, 0.011) | 3.39% | 0.005 (-0.003, 0.015) | 8.36% |
| PTB Test./SHBG          |          | 0.001 (-0.006, 0.009) | 2.52% | 0.002 (-0.004, 0.011) | 2.64% | 0.004 (-0.004, 0.015) | 5.45% |
| PTB SHBG                |          | 0.003 (-0.002, 0.013) | 6.88% | 0.000 (-0.005, 0.005) | NA | -0.001 (-0.008, 0.005) | NA |
| PTB T3                  |          | -0.002 (-0.010, 0.004) | NA | 0.006 (-0.003, 0.019) | 10.0% | 0.008 (-0.001, 0.021) | 15.2% |
| PTB fT4                 |          | 0.001 (-0.005, 0.008) | 1.87% | 0.003 (-0.002, 0.013) | 5.05% | 0.005 (-0.002, 0.017) | 7.45% |
| PTB T4                  |          | 0.001 (-0.004, 0.007) | 0.99% | 0.000 (-0.005, 0.004) | NA | 0.001 (-0.004, 0.007) | 0.30% |
| PTB T3/T4               |          | 0.000 (-0.005, 0.003) | NA | 0.000 (-0.004, 0.004) | NA | 0.000 (-0.009, 0.009) | NA |
| Spont. PTB CRH          |          | 0.010 (0.000, 0.024) | 28.2% | 0.007 (-0.001, 0.020) | 10.8% | 0.008 (-0.001, 0.022) | 13.9% |
| Spont. PTB Estriol      |          | -0.002 (-0.011, 0.005) | NA | -0.001 (-0.005, 0.003) | NA | -0.001 (-0.007, 0.004) | NA |
| Spont. PTB Prog.        |          | 0.006 (0.000, 0.017) | 17.6% | 0.002 (-0.002, 0.010) | 3.32% | 0.003 (-0.001, 0.012) | 5.89% |
| Spont. PTB Prog/E3      |          | -0.001 (-0.009, 0.005) | NA | 0.004 (-0.002, 0.013) | 5.22% | 0.002 (-0.006, 0.012) | 1.45% |
| Spont. PTB Test.        |          | 0.011 (0.002, 0.023) | 30.6% | 0.006 (-0.003, 0.017) | 9.42% | 0.010 (-0.003, 0.026) | 19.4% |
| Spont. PTB Test./SHBG   |          | 0.011 (0.002, 0.025) | 31.1% | 0.006 (-0.002, 0.018) | 9.60% | 0.009 (-0.002, 0.024) | 17.2% |
| Spont. PTB SHBG         |          | 0.003 (-0.004, 0.011) | 6.62% | 0.002 (-0.003, 0.010) | 2.56% | 0.001 (-0.003, 0.006) | 0.84% |
| Spont. PTB TSH          |          | 0.003 (-0.002, 0.011) | 6.20% | 0.003 (-0.006, 0.015) | 5.57% | 0.005 (-0.006, 0.019) | 10.2% |
| Spont. PTB T3           |          | 0.003 (-0.001, 0.010) | 6.90% | 0.002 (-0.003, 0.011) | 3.56% | 0.004 (-0.005, 0.016) | 7.31% |
| Spont. PTB fT4          |          | 0.002 (-0.003, 0.009) | 4.93% | 0.003 (-0.002, 0.012) | 5.36% | 0.004 (-0.005, 0.016) | 7.65% |
| Spont. PTB T4           |          | 0.000 (-0.003, 0.003) | NA | 0.000 (-0.004, 0.003) | NA | 0.000 (-0.004, 0.004) | 0.00% |
| Spont. PTB T3/T4        |          | 0.003 (-0.002, 0.010) | 6.94% | 0.002 (-0.004, 0.010) | 3.02% | 0.003 (-0.005, 0.014) | 5.65% |
| Gest. Age CRH           |          | -0.034 (-0.107, 0.014) | 10.4% | -0.033 (-0.096, 0.009) | 6.78% | -0.021 (-0.087, 0.030) | 5.67% |
| Gest. Age Estriol       |          | 0.032 (-0.030, 0.108) | NA | -0.001 (-0.030, 0.029) | 0.05% | -0.006 (-0.065, 0.052) | 1.24% |
| Gest. Age Prog.         |          | -0.018 (-0.109, 0.074) | 7.30% | -0.030 (-0.089, 0.010) | 6.29% | -0.035 (-0.108, 0.016) | 10.0% |
| Outcome   | Mediator  | NIE (95% CI) | Percent Mediateda | NIE (95% CI) | Percent Mediateda | NIE (95% CI) | Percent Mediateda |
|-----------|-----------|--------------|-------------------|--------------|-------------------|--------------|-------------------|
| PTB       | CRH       | -0.005 (-0.015, 0.002) | NA              | 0.005 (-0.002, 0.018) | 9.97%          | 0.008 (-0.002, 0.023) | 18.9%  |
|           | Estriol   | 0.002 (-0.009, 0.015)  | 2.87%            | -0.003 (-0.014, 0.004) | NA              | -0.004 (-0.015, 0.005) | NA    |
|           | Prog.     | -0.001 (-0.014, 0.013) | NA               | 0.000 (-0.006, 0.006) | 0.15%           | 0.002 (-0.003, 0.010) | 2.23% |
|           | Prog/E3   | 0.000 (-0.004, 0.004)  | NA               | -0.005 (-0.017, 0.002) | NA              | -0.003 (-0.014, 0.003) | NA    |
|           | Test.     | -0.009 (-0.022, 0.000) | NA               | 0.001 (-0.004, 0.009) | 1.55%           | 0.004 (-0.003, 0.014) | 8.61% |
|           | Test./SHBG| -0.006 (-0.019, 0.001) | NA               | 0.001 (-0.003, 0.009) | 1.38%           | 0.004 (-0.005, 0.015) | 7.15% |
|           | SHBG      | 0.003 (-0.003, 0.012)  | 2.70%            | 0.000 (-0.007, 0.006) | NA              | -0.002 (-0.012, 0.007) | NA    |
|           | TSH       | -0.006 (-0.018, 0.002) | NA               | 0.003 (-0.004, 0.013) | 4.11%           | 0.003 (-0.003, 0.013) | 5.34% |
|           | T3        | -0.005 (-0.014, 0.001) | NA               | 0.000 (-0.004, 0.005) | 0.12%           | 0.000 (-0.004, 0.006) | 0.14% |
|           | fT4       | -0.002 (-0.010, 0.005) | NA               | -0.002 (-0.012, 0.006) | NA              | 0.001 (-0.007, 0.008) | 0.83% |
|           | T4        | -0.003 (-0.011, 0.003) | NA               | 0.000 (-0.005, 0.006) | 0.05%           | 0.000 (-0.005, 0.005) | 0.02% |
|           | T3/T4     | -0.003 (-0.012, 0.002) | NA               | 0.000 (-0.005, 0.004) | NA              | 0.000 (-0.005, 0.004) | 0.03% |
| Spont. PTB| CRH       | -0.003 (-0.012, 0.004) | NA               | 0.015 (0.001, 0.036) | NA              | 0.017 (0.001, 0.039) | NA    |
|           | Estriol   | 0.001 (-0.008, 0.011)  | 1.90%            | 0.001 (-0.010, 0.014) | NA              | 0.001 (-0.010, 0.014) | NA    |
|           | Prog.     | -0.001 (-0.011, 0.008) | NA               | 0.006 (-0.001, 0.019) | NA              | 0.005 (-0.002, 0.017) | 5.33% |
|           | Prog/E3   | 0.000 (-0.003, 0.004)  | 0.02%            | -0.002 (-0.013, 0.008) | 2.52%           | -0.005 (-0.018, 0.004) | 2.44% |
|           | Test.     | -0.006 (-0.016, 0.003) | NA               | 0.010 (0.000, 0.026) | NA              | 0.015 (0.002, 0.034) | NA    |
|           | Test./SHBG| -0.003 (-0.013, 0.006) | NA               | 0.011 (0.000, 0.028) | NA              | 0.015 (0.002, 0.034) | NA    |
|           | SHBG      | 0.002 (-0.003, 0.010)  | 2.63%            | 0.004 (-0.003, 0.016) | NA              | 0.003 (-0.005, 0.014) | NA    |
|           | TSH       | -0.003 (-0.011, 0.003) | NA               | 0.006 (-0.003, 0.020) | NA              | 0.006 (-0.002, 0.019) | NA    |
|           | T3        | -0.003 (-0.010, 0.001) | NA               | 0.005 (-0.003, 0.017) | NA              | 0.007 (-0.002, 0.020) | NA    |
| Variable | Estimate | CI (Lower, Upper) | p-value | Percent Mediated | Estimate | CI (Lower, Upper) | p-value | Percent Mediated | Estimate | CI (Lower, Upper) | p-value | Percent Mediated |
|----------|----------|------------------|---------|------------------|----------|------------------|---------|------------------|----------|------------------|---------|------------------|
| fT4      | 0.000    | (-0.005, 0.004)  | NA      | 0.001            | (-0.006, 0.010)  | NA      | 0.004            | (-0.002, 0.014)  | NA      | 0.006            | (-0.003, 0.018)  | NA      |
| T4       | -0.002   | (-0.009, 0.003)  | NA      | 0.000            | (-0.007, 0.005)  | 0.44%   | 0.000            | (-0.004, 0.005)  | 0.18%   |
| T3/T4    | -0.002   | (-0.009, 0.002)  | NA      | 0.005            | (-0.004, 0.019)  | NA      | 0.006            | (-0.003, 0.018)  | NA      |
| Gest. Age| CRH      | 0.007            | (-0.030, 0.055) | NA | -0.022           | (-0.091, 0.031) | 4.92% | -0.013           | (-0.228, -0.010) | 38.3% |
|          | Estriol  | 0.002            | (-0.063, 0.071) | NA | 0.001            | (-0.023, 0.030) | 0.27% | -0.011           | (-0.078, 0.047) | 2.12% |
|          | Prog.    | -0.006           | (-0.100, 0.086) | 1.62% | 0.038            | (-0.010, 0.108) | NA | -0.015           | (-0.086, 0.044) | 5.72% |
|          | Prog/E3  | -0.003           | (-0.041, 0.033) | 0.18% | 0.043            | (-0.010, 0.122) | NA | 0.047            | (-0.015, 0.134) | NA |
|          | Test.    | 0.021            | (-0.027, 0.084) | NA | -0.001           | (-0.040, 0.037) | 0.41% | -0.047           | (-0.140, 0.016) | 14.9% |
|          | Test./SHBG| 0.012           | (-0.030, 0.068) | NA | 0.001            | (-0.034, 0.037) | 0.13% | -0.044           | (-0.130, 0.022) | 14.5% |
|          | SHBG     | -0.002           | (-0.033, 0.024) | 0.18% | 0.003            | (-0.022, 0.035) | 0.22% | -0.006           | (-0.062, 0.045) | 1.00% |
|          | TSH      | 0.001            | (-0.036, 0.039) | NA | -0.029           | (-0.098, 0.011) | 2.86% | -0.040           | (-0.123, 0.009) | 11.8% |
|          | T3       | 0.009            | (-0.026, 0.056) | NA | 0.000            | (-0.027, 0.029) | 0.24% | 0.000            | (-0.051, 0.051) | 0.04% |
|          | fT4      | -0.013           | (-0.077, 0.047) | 2.48% | 0.005            | (-0.035, 0.051) | 0.46% | -0.019           | (-0.081, 0.020) | 4.15% |
|          | T4       | 0.023            | (-0.019, 0.081) | NA | 0.005            | (-0.024, 0.041) | 0.15% | 0.001            | (-0.030, 0.034) | 0.14% |
|          | T3/T4    | 0.003            | (-0.030, 0.043) | NA | 0.005            | (-0.022, 0.045) | 0.07% | 0.009            | (-0.042, 0.068) | NA |

*Indication is NA when the TE and NIE are in different directions, rendering the percent mediated uninterpretable. Estimates refer to the increase in probability of experiencing binary outcomes, or the unit change in continuous outcomes, due to the resulting change in the mediator with an interquartile range increase in exposure, while holding the exposure constant. Boldface text indicates a p-value < 0.1.